PLACENTAL PATHOLOGY IN LOW BIRTH WEIGHT LIVE BIRTHS

Dissertation submitted in

Partial fulfillment of the regulations required for the award of

M.D. DEGREE

in

PATHOLOGY – BRANCH III

The Tamil Nadu

Dr. M.G.R. Medical University

Chennai

APRIL – 2012

CERTIFICATE

This is to certify that the dissertation entitled **"Placental Pathology in Low Birth Weight Live Births"** is a bonafide work done by **Dr.S.Yogalakshmi**, Post Graduate student in the Department of Pathology, Coimbatore Medical College, under the supervision and guidance of **Dr.M.Murthy, M.D,** Professor & Head, Department of Pathology, Coimbatore Medical College, Coimbatore, in partial fulfillment of the requirement of The Tamilnadu Dr.M.G.R.Medical University for the award of M.D. Degree in Pathology.

Prof. Dr. R. Vimala, M.D.,
Dean,
Coimbatore Medical College
Coimbatore.

Prof. Dr. M. Murthy, M.D.,
Professor& Head, Dept. of Pathology,
Coimbatore Medical College
Coimbatore

DECLARATION

I, **Dr.S.Yogalakshmi** solemnly declare that dissertation titled, **"Placental Pathology in Low Birth Weight Live Births"** is a bonafide work done by me at Coimbatore Medical College during 2009 - 2012 under the guidance and supervision of **Prof. Dr. M. MURTHY, M.D.,** Professor and Head, Department of Pathology, Coimbatore Medical College, Coimbatore.

The dissertation is submitted to The Tamilnadu Dr.M.G.R. Medical University, towards partial fulfillment of requirement for the award of **M.D. Degree in Pathology (BRANCH – III).**

Place : Coimbatore **Dr.S.YOGALAKSHMI**

Date :

ACKNOWLEDGMENT

I wish to record my sincere gratitude to our respectful Dean, **Professor. Dr.R.Vimala, M.D.,** Coimbatore Medical College, Coimbatore for permitting me to carry out this study and to avail all the facilities in this institution.

I am deeply indebted to our **Professor. Dr. M.Murthy, M.D.,** Professor& Head of the Department of Pathology, Coimbatore Medical College, Coimbatore, but for whose guidance, this study would not have come through. It has been a great privilege to work under him and especially on this topic.

I am thankful to our Associate Professors **Dr.Arjunan, M.D.,** and **Dr.C.Lalitha, M.D**., for their timely help and guidance.

I express my profound gratitude to **Dr.Dhanalakshmi, M.D.,** Associate Professor for her valuable guidance and support.

I wish to record my sincere thanks to all the Assistant Professors of our department for their constant support and encouragement.

I take this opportunity to my fellow Post Graduates and all the Technical Staff of our department for their contribution to this study.

This study would not have seen the light of the day, had not our patients showed the kind cooperation they extended. I sincerely thank them.

CONTENTS

LIST OF COLOUR PLATES

20	Fibrinoid Necrosis - Microscopic Picture
21	Basement Membrane Thickening - Microscopic Picture
22	Avascular Villi - Microscopic Picture
23	Distal Villous Hypoplasia - Microscopic Picture
24	Sub Chorionic Micro Abscess - Microscopic Picture
25	Acute Chorioamniotis - Maternal Inflammatory Response Stage 1 - Microscopic Picture
26	Chorionic Intervillositis - Microscopic Picture
27	Vestigial Remnant - Microscopic Picture

LIST OF TABLES

LIST OF CHARTS

ABBREVIATION

1.	NICU	-	Neonatal Intensive Care Unit
2.	PIH	-	Pregnancy Induced Hypertension
3.	LBW	-	Low Birth Weight
4.	IUGR	-	Intra Uterine Growth Retardation
5.	SGA	-	Small for Gestational Age
6.	PVF	-	Perivillous Fibrin
7.	IVH	-	Intra Villous Hemorrhage
8.	GDM	-	Gestational Diabetes Mellitus
9.	BM	-	Basement Membrane
10.	VSM	-	Vasculo Syncytial Membrane
11.	IHC	-	Immuno Histo Chemistry

PLACENTAL PATHOLOGY IN LOW BIRTH WEIGHT LIVE BIRTHS

ABSTRACT

Aim - To study the various pathological changes (both gross and histological) that occur in the placentas of low birth weight live births.

Objectives- To study the gross morphological and histological appearance of placentas of low birth weight live births and to derive a probable etiology for low birth weight, based on placental pathology.

Materials and methods- It is a Prospective Study from September 2009 to September 2011 carried out in Coimbatore Medical College and Hospital. 50 placentas expelled during normal delivery or caesarean section were subjected to pathological examination. Detailed history of the mother was recorded and results were analyzed.

Results- Pregnancy induced hypertension and anemia are the most common conditions that produce low placental weights and low birth weight (LBW) live births. Placental morphological changes increase in direct proportion to the severity of diseases. Membrane opacities (48%), perivillous fibrin deposit (46%) and placental infarcts are the most commonly observed gross morphological changes. Syncytial knots (88%) and fibrinoid necrosis (88%) are the most common histological finding. Increased syncytial knot formation is a consistent feature of anemia and Pregnancy induced hypertension and increased basement membrane thickness is a common finding in severe anemia.

Keywords - Syncytial knots, fibrinoid necrosis, perivillous fibrin deposit and placental infarct.

INTRODUCTION

Placenta is the only organ to develop in adulthood and is the only organ with a defined end state. The structure of the placenta has a strong relation with pregnancy length, physical milieu of mother and a resemblance to the concept of ‘imhotep’ (regarded as the first medicolegal expert) showing relation between forensic medicine histology, morphology and pathology.

In an era of immortality due to the advance nanotechnology the wonder organ i.e., the placenta in the preserved state can relate foetal outcome with its histomorphology.

Even now, in an era of advanced medical care the incidence of low birth weight and birth defects in the newborn is a major health problem in our country. This also may cause great financial stress to the parents as well as health care system, due to prolonged treatment in NICU. The etiological factor for fetal growth retardation include maternal malnutrition, anaemia, preeclampsia, maternal infection, drug abuse, genetic factors and genetic diseases, congenital malformation, multiple gestations, placental and cord abnormalities. The risks of hypertension, coronary artery disease and diabetes mellitus are inversely related to birth weight and lower values in anthropometry in newborn.

The first study of growth rate of normal human foetuses and their placenta, to ascertain their interrelationship through the stages of intrauterine life, was done by Henricks and subsequently by Boyd and Hamilton.

There are later studies to suggest that placental volume in the second trimester can predict birth weight and newborn anthropometry and identify the fetus in danger of being low birth weight.

Much research work has been done on the placental weight and fetoplacental weight ratios at different gestational ages. Results vary considerably depending upon the methods used in handling the placenta.

Relations between birth weight, placental surface area and placental volume have been described in normal term pregnancies and preterm pregnancies. There is little available information about placental dimensions in small for gestational age babies.

During the past few years, the placenta has however increasingly attracted the attention of workers from wide range of scientific disciplines.

To overview all these studies, it is clear that placental pathology may have an impact on long term development on the baby and may also impart a scope for prevention of certain morbidities in subsequent pregnancies.

In general, neonates weighing less than 2.5 Kg at birth are termed as low birth weight (both preterm and term). In both groups, pathological examination of the placenta may reveal the causes of low birth weight, and gives useful insight into the diagnosis and treatment of sick newborns and reflects the impact of maternal disorders of pregnancy.

This study focuses on, the morphological appearance of the placenta in relation to the low birth weight live births, and the pathological changes in the various placentas collected from high risk mothers, as well as normal mothers who had delivered low birth weight live babies.

AIM OF THE STUDY

To study the various pathological changes (both gross and histological) that occur in the placentas of low birth weight live births collected from our hospital, and to obtain a probable etiological causes for low birth weight live births.

OBJECTIVES

- To study the gross morphological appearance of placentas of low birth weight live births as well as normal live births.
- To study the histopathological appearances of placentas of low birth weight live births.
- To study the various histological changes that occurs in high risk pregnancies like anemia and PIH.
- To analyse all the data and to derive a probable etiology for low birth weight.

NEED FOR THE STUDY

Despite the growing scientific interest of neonatology for the placenta, it was observed that there are still few works in the literature approaching the subject in a multidisciplinary way. Although intrauterine growth is determined by several factors, there are relatively few multidisciplinary studies relating placental disorders to specific groups of low birth weight live births.

To study the role of the placentas in the birth of low birth weight live births is to look for the disorders that may be directly or indirectly associated with the etiopathogenesis of intrauterine growth retardation.

Even though numerous studies in literature have analysed the role of placenta in the low birth weight live births, scientific papers from our country were very few. So it was to study the above mentioned subject and to draw a conclusion about the role of placenta in the low birth weight live births.

REVIEW OF LITERATURE

PLACENTAL DEVELOPMENT

Implantation occurs on post ovulation day 6-7; by day 10, the ovum is implanted in the endometrial stroma .Vessels develop from extraembryonic mesenchyme and the placenta is vascularized by day twenty one. Villous vessels appear at 6 weeks; At 8 weeks they contain nucleated red blood cells (nRBC)and by 10 weeks they have 10% nRBC. nRBC becomes absent at 12 weeks.

The primary stem villi breakup just below the chorionic plate into a number of secondary stem villi.

Secondary Stem villi after running for a short distance parallel to the chorionic surface divide into a series of tertiary stem villi.

Tertiary Stem villi which form the lobules, sweep down through the intervillous space towards the basal plate into which they insert & then turn back upon themselves to re-enter the intervillous space. Here they breakup into branches which form the terminal villous network. Branches are given off directly from tertiary stem villi during their downward course toward basal plate.

The lobule can receive tertiary stem villi from a number of secondary stem villi and adjacent lobules are usually separated by interlobular areas which are in continuity with the Subchorial Lake.

Villi in first trimester: 170 microns (large), outer layer of syncytiotrophoblast and inner cytotrophoblast, loose stroma with primitive fibroblasts and Hofbauer cells (macrophages) are plentiful, vessels are small and centrally placed and contain only nucleated red blood cells

Villi in second trimester: 70 microns, primarily syncytiotrophoblasts, cytotrophoblast layer is attenuated, villi contain collagen and numerous vessels; stroma is more compact.

Villi in third trimester: smaller than second trimester; syncytiotrophoblast knots in 30%, dilated fetal capillaries fuse with syncytiotrophoblast to form vasculosyncytial membranes, stroma is reduced to thin strands; trophoblastic inclusions are common.

The expelled placenta appears as a discoid mass which weighs about 450 gm., and has a diameter of from 15 to 20 cm. Its average thickness is about 3 cm, but this diminishes rapidly toward the circumference of the disk, which is continuous with the membranes. Its uterine surface is divided by a series of fissures into lobules or cotyledons, the fissures containing the remains of the septa which extended between the maternal and fetal portions. Most of these septa end in irregular or pointed processes; others, especially those near the edge of the placenta, pass through its thickness and are attached to the chorion. In the early months, these septa convey branches of the uterine arteries which open into the intervillous space on the surfaces of the septa. The fetal surface of the placenta is smooth, being closely invested by the amnion.

Seen through the latter, the chorion presents a mottled appearance, consisting of gray, purple, or yellowish areas. The umbilical cord is usually attached near the center of the placenta, but may be inserted anywhere between the center and the margin; in some cases it is inserted into the membranes, i.e., the velamentous insertion. From the attachment of the cord, the larger branches of the umbilical vessels radiate under the amnion, the veins being deeper and larger than the arteries. The remains of the vitelline duct and yolk-sac may be sometimes observed beneath the amnion, close to the cord, the former as an attenuated thread, the latter as a minute sac. The fetal placenta is formed by a number of subunits (about 200) called lobules.

Membranes: They usually insert directly into placental edge. Membrane layers are amnion, exocoelomic space, chorion, decidual capsularis.

Amnion: Innermost covering of amniotic cavity; flat epithelial cells resting on basement membrane; squamous metaplasia is common, especially near the insertion of cord.

Exocoelomic space: Between amnion and chorion; usually obliterated, but causes membranes to slide against each other

Chorion: Connective tissue membrane containing fetal vessels, internal to amnion, external to villi.

Chorion laeve: Chorion associated with the membrane and not with the decidua basalis; villi are oriented toward the uterine cavity, but atrophy to form the smooth (laeve) chorion; trophoblasts are vacuolated

Chorion frondosum: Chorion associated with the decidua basalis, located in the placenta proper

Basal plate: Portion of the placenta attached to the uterus

Chorionic plate: Portion of the placenta closest to the fetus.

Cotyledon: Grossly noted unit of placenta, from primary stem villi

Lobule: functional subunit from secondary stem villi

Basic Villous Structure:

1. Villous Trophoblast:

The outer surface of villi is covered by a trophoblastic mantle – consists of 2 easily distinguishable layers, an outer layer of Syncytiotrophoblast and Inner layer of cytotrophoblast (Langhan's cells)

Cytotrophoblast:-

Cuboidal, polyhedral or ovoid cells, have well marked cell borders. Their cytoplasm is clear or slightly granular, nucleus is pale staining with a finely dispersed chromatin network. In early pregnancy, they are prominent & forms a complete layer. They are less conspicuous in the terminal villi of mature placenta, tend to be flattened between syncytiotrophoblast & basement membrane. They are dispersed and do not form a complete layer. They are the stem cells & in late pregnancy represent an inactive 'germinative' layer.

Syncytiotrophoblast:-

No cell boundaries are visible between the nuclei of Syncytiotrophoblast. In early Pregnancy, they form a layer of uniform thickness, nuclei are regularly spaced, smaller and darkly staining, cytoplasm may be homogenous or finely granular, sometimes vacuolated. In term

placenta, the syncytial nuclei are irregularly dispersed, aggregated to form multinucleated protrusions from villous surface, being known as syncytial knots.

Vasculosyncytial membrane:

In some areas of many villi of the mature placenta, the syncytiotrophoblast is focally thinned out and anuclear. They overlie a dilated fetal capillary and on light microscopy appear to fuse with the vessel wall; they are specialized zones of the trophoblast for the facilitation of gas transfer. They are considered as morphological evidences of functional topographic differentiation of the trophoblast

2. Trophoblastic Basement Membrane:

Villous trophoblast is separated from the underlying stroma by the trophoblastic basement membrane. It has fibrillary structure (20 -50nm thick). Main Components – Collagen IV, laminin & Heparan Sulphate.

3. Villous Stroma:

It contains-Undifferentiated mesenchymal cells, Mature mesenchymal (reticulum) cells, Fibroblasts, Myofibroblast, Procollagen & collagen fibers; the relative proportions vary with gestational age & stage of development of the villous tree. Few mast cells, Hofbauer cells are also present in the villous stroma.

Hofbauer cells:

They are round, ovoid or reniform shape. They have eccentrically placed nuclei and the cytoplasm is vacuolated .They present at a very early stage of development & persist throughout the pregnancy. They are capable of both immune and Nonimmune phagocytosis, can trap maternal antibodies crossing over into the placental tissues.

4. Fetal villous vessels:

The vessels in the terminal villi of the mature placenta are of capillary size, many appear sinusoidally dilated

Intermediate (extravillous) trophoblast

X cells

They infiltrate the decidua and myometrium, invade and replace the spiral arteries of the basal plate to establish maternal-fetal circulation and keep the vessels patent. They form the trophoblastic shell, present in villi and membranes. They are more prominent at the implantation site.

Villous intermediate trophoblast

They are present in trophoblastic columns adjacent to villus.

Microscopic Appearance: They are larger than cytotrophoblasts, polygonal in shape with abundant clear or eosinophilic cytoplasm, distinct cell border and a single nuclei

Implantation site intermediate trophoblast

They infiltrate the endomyometrium of the placental site

Microscopic Appearance: Enlarged polyhedral to spindle cells with abundant amphophilic and vacuolated cytoplasmic and large, hyperchromatic nuclei. They resemble adjacent decidua and in the myometrium, they are more spindled and resemble adjacent smooth muscle cells. They may fuse to become multinucleated cells.

Temporal Variation in villous structure:

Growth & Maturation of the villous tree:

1. Mesenchymal Villi:

Transient stage in placental development. They comprise the 1st generation of newly formed villi and are derived from trophoblastic sprouts by mesenchymal invasion & vascularisation

i. Mainly seen in early stages of pregnancy, but few may be found in the center of the lobules at term.
ii. Can differentiate into either mature or intermediate villi
iii. They have complete trophoblastic mantles with many cytotrophoblastic cells and regularly dispersed nuclei in the syncytiotrophoblast.
iv. Stroma is loose,of immature type and abundant, containing few Hofbauer cells together with poorly developed fetal capillaries.

2. Immature Intermediate Villi

i. These are peripheral extensions of the stem villi

ii. They are the predominant form seen in immature placentas and often persist in small groups in the centres of the lobules in mature placentas representing a persistent growth zone.

iii. They have well presented trophobalstic mantle with numerous cytotrophoblasts. The Syncytial nuclei are evenly dispersed and there are no Syncytial knots or Vasculosyncytial membranes.

iv. They have an abundant loose stroma that contains many Hofbauer cells. Capillaries, arterioles and venules are present.

3. Stem Villi:

i. Comprise the primary stems which connect the villous tree to the chorionic plate.

ii. Serve as scaffolding for the peripheral villous tree & it makes up 1/3 of total volume of villous tissue in mature placentas.

iii. Predominant in the central subchorial portion of the villous tree

iv. Microscopically they have a compact stroma & contains arterioles, venules & Capillaries.

4. Mature Intermediate Villi:

i. These are the peripheral ramification of villous stems

ii. They are large (60-150μm) and contain capillaries admixed with small arterioles and venules in very loose stroma.

iii. Occupies more than 1/2 of villous volume.

iv. Syncytiotrophoblast – has uniform structure. No knots or vasculo – Syncytial membranes are present

v. Occupies ¼ villous type.

5. Terminal Villi:-

Appear at about 27weeks of gestation, grape like outgrowths from mature intermediate villi, contains 5-6 capillaries, irregularly spaced syncytial nuclei, syncytial knots may be present, occupies 30-40% of villous volume.

Umbilical cord

Umbilical cord-normal

55-65 cm long with outer amniotic epithelium. Bulk is composed of mucoid Wharton's jelly, 2 arteries and 1 vein, although 2 arteries often merge near the end of cord. Diameter is 1 cm or more with Central insertion into placenta at mid gestation. Insertion may become more eccentric as gestation proceeds

Umbilical arteries: Double layered muscular wall, no internal elastic lamina

Umbilical vein: Larger diameter has thin wall with single layer of disorganized circular smooth muscle and an internal elastic lamina; no intimal layer is in.

Mean placental weight by gestational age:

Prior to 28 weeks	253 grams
28-32 weeks	314 grams
33-36 weeks	391 grams
37-40 weeks	456 grams
>40 weeks	496 grams

Abnormalities of placentation and of placental development

Accessory (succenturiate) lobe

Present in 3% of placentas and often attached by fetal membranes. Vasculature between the lobes is unsupported by placenta and they are at risk for fetal hemorrhage and thromboemboli.

Bilobate placenta

2 lobes of equal size, separated by fetal membranes or connected by narrow isthmus of placental tissue. It has uncertain clinical significance, but at risk of fetal bleeding from velamentous/intramembranous vessels. Maternal postpartum bleeding occurs if a portion is retained in utero.

Circumvallate placenta

Placenta with extrachorial part; chorion is folded or rolled back on itself and has a peripheral protuberance. It is associated with low birth weight babies, marginal hemorrhage and is more common in multigravidas. If cysts and other gross aberrations are present, this may be associated with fetal and maternal abnormalities

Circummarginal placenta

Extrachorial placenta with thin and flat margin. It has minimal clinical significance, more common in multigravidas.

Macroscopic Abnormalities of the placenta:

I. Lesions due to disturbances of maternal blood flow:

A) Perivillous fibrin deposition:

Gross: Fibrin – Eosinophilic, amorphous material derived from maternal blood in the intervillous space. Plaques of perivillous fibrin are most frequently seen in peripheral part of placenta. In some it occurs in the more central portion as an irregular vertical strip running between maternal & fetal surface as circular (or) ovoid plaque in basal or intermediate zones. It is hard, irregular in outline and sharply demarcated with whitish cut surface.

Microscopic Appearance: Widely separated terminal & stem villi entrapped in fibrin which is completely obliterating the intervillous space. In fresh lesions, few degenerated syncytial nuclei, slightly thickened trophoblastic basement membrane are seen. In older plaques, the syncytiotrophoblast of the involved villi disappears and trophoblastic basement membrane is thickened. Progressive fibrosis of the stroma with sclerosis & villous vessels are seen. The cytotrophoblast proliferates forming a prominent mantle around individual villi. When more than 30% of villous parenchyma is involved it is called as massive perivillous fibrin deposition. IUGR is seen in 1/3rd cases.

Massive perivillous fibrin deposition & maternal floor infarction may represent a spectrum of the same underlying pathophysiological process[(1).]

Fibrin deposition is due to thrombosis of maternal blood as a result of eddy current and stasis within the intervillous space.

B) Subchorionic fibrin plaque:

Gross: Laminated white plaque, roughly triangular with the base of the triangle fused with the under surface of chorionic plate and the apex protruding into the placental substance. The fibrin plaques are sharply demarcated from normal placental tissue.

Microscopic Appearance: Laminated fibrin in which no villi are present. The fibrin is intimately attached to the under surface of the chorionic plate. Massive subchrionic fibrin deposition may be associated with intrauterine growth retardation[(2)].

C) Maternal floor infarction:

Excess deposition of fibrin on the basal plate of the placenta[(3)].

Gross: Maternal surface has a gyriform appearance & is greyish yellow colour. The basal plate is markedly thickened by firm white material and in strands extending towards chorionic plate giving a ‘marbled’ appearance.

Microscopic Appearance: Excess fibrin deposited on the basal plate of the intervillous space and basally situated villi are often entrapped with the enlarging fibrinous mass.

- Increased amounts of pregnancy associated major basic protein are present in the lesions of maternal floor infarction.
- Maternal floor infarction is associated with a high incidence of fetal death and intrauterine growth retardation[(4)].

4) Infarct:

It is a localized area of ischemic villous necrosis.

Gross: It is more common in peripheral areas. It is variable in shape with base abutting onto the basal plate. Fresh infarct is dark red & as it ages it becomes firm to hard, white plaque with a smooth or slightly granular surface, occasionally calcification may be seen.

Microscopic Appearance: In early infarct: Crowding of villi with narrowing or obliteration of the intervillous space. Villous vessels are dilated and congested. Syncytial nuclei shows pyknosis or karyorrhexis.

In old infarct: Trophoblast disappears with thin rim of acidophilic hyaline material around the perimeter of each villous. Stroma is degenerated. This coagulative villous necrosis results in crowded ghost villi.

The incidence of infarction is increased in pregnancies complicated by preeclampsia (or) essential hypertension[5]. Extensive placental infarction is associated with a high incidence of fetal hypoxia, IUGR and fetal death.[6]

Lesions due to disturbances of fetal blood flow:

Fetal artery thrombosis (fetal thrombotic vasculopathy)

Thrombotic occlusion of a chorionic (or) major fetal villous stem artery produces a sharply delineated area of villous avascularity.

Gross: Roughly triangular and well delineated area of pallor within the placental substances with its base abutting onto the basal plate.

Microscopic Appearance: Sharply demarcated area of the avascular villi is seen. Markedly excessive formation of syncytical knots is also usually seen. Trichrome stain shows excessive amount of stomal fibrosis. Hemosiderin deposition in villi may be seen. The stem vessels distal to the occlusion show a well-marked fibromuscular sclerosis.

Fetal artery thrombosis is secondary to a diminished maternal blood flow with slowing, and eventual thrombosis, of blood in the fetal vasculature[7]. Placentas showing more avascular villi per section are diagnosed as fetal thrombotic vasculopathy. (Redline et al 2008)[8]

An association between fetal thrombotic vasculopathy and maternal hemolytic uraemic syndrome in pregnancy has been reported (Hebisch et al 2001)[9].

Thrombi & Haematomas:

Massive subchorial thrombosis: (Breus' mole)

A red thrombus measuring more than 1 cm in thickness separates the chorionic plate from the underlying villous tissue.

Microscopic appearance: Confined to the subchorionic space. Laminated thrombosis, no villi are included within it. 2 cases of massive subchorial haematomas were reported following thrombolytic therapy in pregnant patients with prosthetic heart valves (Usta et al 2004)[10]. Heller et al (2003)[11] have reported, 3 examples of massive subchorial haematomas occurring in women with thrombophilic conditions.

Retroplacental Haematoma: It has haematoma between the basal plate of the placenta and uterine wall. It is associated with the clinical syndrome of placental abruption, manifesting as antepartum haemorrhage.

Gross: Freshly formed haematoma is soft, red and easily separated from maternal placental surface & compresses the overlying placental parenchyma. The older haematoma is brown, hard and firmly adherent to the placental surface.

Microscopic Appearance: In early stages, haematoma consists of RBC with few strands of fibrin. In older lesions erythrocyte degeneration and fibrin appears in increasing amounts. They are infiltrated by neutrophils and macrophages.

Clinical placental abruption is usually quoted as occuring in 0.5 – 1% of pregnancies (Ananth et al 2004)[12]

Pregnancy associated hypertensive disease is an important risk factor for abruption (Sheiner et al 2003)[13]. Increased frequency of methylenetetrahydrofolate reductase (MTHFR) mutations has been reported in association with placental abruption (Parle McDermoH et al 2005)[(14)]. Cigarette smoking is associated with a doubling risk for abruption(Ananth et al 1999)[(15)]

Women with anticardiolipin antibodies, hyperhomocysteinemia and other prothrombotic tendencies are associated with increased incidence of abruptio placenta (Jaaskelainen et al 2004)[16]

Placental abruption associated with chorioamnionitis is attributed to bacterial colonization of the decidua with resultant inflammation and damage to decidual vessels (Darby et al 1989)[17]

Neonates born after a placental abruption have increased rates of clinically significant periventricular leucomalacia and haemorrhage (Gibbs & Weindling 1994)[18]

Retroplacental haematomas found in first trimester scanning were associated with subsequent complication like pregnancy induced hypertension, pre-eclampsia, clinical placental abruption, antepartum hemorrhage, preterm delivery, fetal growth restriction, fetal distress & neonatal intensive care unit admission (Nagy et al 2003)[19].

Marginal Haematoma:

It is a haematoma formed at the lateral margin of the placenta.

Microscopic Appearance: Coagulum lies outside the intact lateral wall of the placenta. Harris (1988)[20] has claimed that there is a significant relationship between marginal haematomas and premature onset of labour.

Intervillous thrombi: Villous free nodular foci of coagulated blood in the intervillous space.

Gross: May be round (or) oval in shape, can occur in any part of placental substance. A fresh intervillous thrombus is soft and dark red. As the thrombus ages, a hard, white sharply delineated, laminated plaque is formed.

Microscopic Appearance: Freshly formed thrombus consists predominantly of red blood cells, as thrombus ages red blood cells gradually degenerate and laminated fibrin is progressively laid down.

A careful study of fresh intervillous thrombi reveal the presence of nucleated red blood cells.

Kline's haemorrhage: It consists of a nodular focus of semi-fluid or fluid blood within the placental parenchyma.

Sub amniotic haematoma: It is a collection of free blood lying between amnion and chorion on the fetal surface of the placenta. Desa (1971)[(21)] noted an association between the presence of older haematomas and a low birth weight. He found that these haematomas were accompanied by evidence of old thrombi in the chorionic veins. Subamniotic haematomas are often associated with raised maternal serum alpha-fetaprotein concentration (Van Den et al 2000)[(22)]

NON VASCULAR LESIONS:

Calcification: Gross: Seen on the maternal surface as small, hard, scattered flecks principally in the basal plate and in the septa. They are seen in old infarcts and in plaques of perivillous or subchorial fibrin.

Microscopic Appearance: Structureless, basophilic material deposited as plaques or as coarse granules which are strongly PAS positive and give positive reaction with Von Kossa's stain.

Gross calcification is distinctly uncommon in placenta from pregnancies terminating before the 36th week of gestation. Maternal smoking is associated with increased placental calcification (Klesges et al 1998)[(23)]. Massive extensive placental calcification may be associated with underlying maternal disease such as hyperparathyroidism (Graham et al 1998)[(24)].

Septal cyst:

Is a round (or) oval cyst, sharply demarcated, 5-10 mm in diameter. The cyst wall is formed by smooth, thin, glistening membrane and the cyst contents are grey and gelatinous. The cyst is usually seen in the subchorionic zone and often the cyst walls are in direct continuity below with a septum. The cysts occur more commonly in oedematous placenta and are therefore more frequently found in those from diabetic women or from cases of maternal-fetal Rhesus incompatibility.

Some gross lesions are significant as a direct cause of fetal death, hypoxia or growth retardation, these including very extensive perivillous fibrin deposition, maternal floor infarction, multiple fetal artery thrombi and large

retroplacental hematomas. Infarction when extensive, serves as an indicator of a markedly abnormal maternal vasculature while the presence of a fetal artery thrombosis may be associated with thrombi elsewhere in the fetal vasculature.

Histopathological abnormalities of the placenta:

Abnormalities of the trophoblast:

Excessive number of syncytical knots:

Syncytial knots are focal clumps of apoptotic syncytial nuclei that protrude into the intervillous space from the surface of the villi.

Beyond 32nd week of gestation they increase in number until term at which time knots are normally present on 11 to 30 percent of villi. Formation of knots on more than a third of the villi is considered excessive. Localised excess of knots is seen in avascular villi due to fetal artery thrombosis and in those villi adjacent to an infarct which are poorly perfused because of fibromuscular sclerosis in the fetal stem artery. Excessive formation is a feature of placenta from pregnancies complicated by preeclampsia and intrauterine growth restriction (Hansen et al 2000)[(25)] as well as in placenta delivered from women living at high altitude during pregnancy (Khalid et al 1997)[(26)].

Excessive synctial knots are an indication of uteroplacental ischemia (the 'Tenney-Parker Change') or fetal stress (Benirschke and Kaufmann 2000)[(27)].

Diminished fetal perfusion of the villi leads to their collapse with increased incidence of artefactual tangential cutting of trophoblastic tissue.

Excessive number of villous cytotrophoblastic cells:

Villous cytotrophoblastic cells becomes less prominent as pregnancy proceeds and in mature villi they tend to be flattened and presence of these cells are feature of the prematurely delivered placenta. Numerous villous cytotrophoblastic cells are a striking feature of placentas from diabetic women, cases of materno-fetal Rhesus incompatibility and pre-eclampsia (Burkshee et al 1974)[28]. An excess of villous cytotrophoblastic cell is a feature of plancentas from infants with idiopathic intrauterine growth retardation and from women who smoke during pregnancy (Demir et al 1994)[29]

Increased thickness of the trophoblastic villous mantle impairs the oxygen transfer capacity of the placenta (Salafia et al 1995)[30]

Deficiency of vasculo-syncytial membranes:

Vasculo-syncytial membranes are specialized areas of the syncytiotrophoblast which appear to be specifically adapted for transfer purposes and their presence is an indication of topographic functional differentiation of the trophoblast . A vasculo-syncytial membrane consists of attenuated anuclear vasculo-syncytium stretched over in close apposition with a sinusoidally dilated vessel. Beyond 32nd week of gestation, it increases rapidly and at term it is present on about 20% of the villi. If <5% of these are seen in term villi, it is considered as deficiency of vasculo-syncytial membranes.

There is an inverse relationship between the villous vasculo-syncytial membranes and fetal hypoxia (Fox 1967 a)[31]. Unduly low number of vasculo-syncytial membranes is seen in pre-eclampsia,materno-fetal Rhesus incompatibility and in placentas from infants of low birth weight and from fresh stillbirths. Paucity of villous vasculo-syncytial membranes occurs in retardation of villous maturation, failure of fetal villous perfusion and failure of trophoblastic differentiation.

Fibrinoid necrosis of villi:

A small nodule of homogenous, acidophilic, PAS-positive material appears at one point in the villous trophoblast. This nodule progressively enlarges as fresh fibrinoid material which bulges into the villous stroma. The whole villous is converted into a fibrinoid nodule. Few remnants of syncytiotrophoblast remain around the periphery of fibrinoid material in late stages. This is not due to deposition within the villous of fibrin derived from the maternal blood in the intervillous space (Wilkin 1965[32]); why it develops is far from clear. It is the visible hallmark of an immunological reaction within trophoblastic tissues.

In a study of 220 placentas from term uncomplicated pregnancies there were none in which more than 3% of villi had undergone complete fibrinoid necrosis (Fox 1968 a)[33]. Any placenta in which more than 3% of villi showed fibrinoid necrosis is considered abnormal; villous fibrinoid necrosis is high in prematurely terminating pregnancies. Increased frequency of villous fibrinoid necrosis is seen in the placentas of low birth weight infants (Gershon

& Strauss 1961)[34] with pre-eclampsia and materno-fetal Rhesus incompatibility and (Mayhew & Sampson (2003)[35] .

ABNORMALITIES OF THE TROPHOBLASTIC BASEMENT MEMBRANE:

Increase in its thickness and Excessive basement membrane mineralization

Excessive mineralization in H&E stained sections is seen as Haematoxophilic finely granular material in a linear pattern of the trophoblastic basement membrane. Excessive mineralization is reported in association with fetal demise, fetal abnormalities such as anencephaly, fetal aneuploidies such as trisomies, rare metabolic disease such as fetal bartter syndrome and in the villi distal to a fetal stem artery occlusion. (Mc Dermott & Gillan 1995; Roberts et al 2000; Ernst and Parkash 2002)[36 - 38].

Increased mineralization is also reported in association with the administration maternal corticosteroid therapy to accelerate fetal lung maturity (Ghidini et al 2001)[39]

Increased thickness is easily assessed in PAS-stained sections. More than 3% of villous population with thickened trophoblastic basement membrane is abnormal (Fox 1968 C)[40]. This is seen in placentas from women with pre-eclampsia, essential hypertension or intrauterine growth restriction. Also increased thickness of membrane is observed in placentas from women with diabetes mellitus, from cases of materno-fetal Rhesus incompatability

and from women who smoke during pregnancy (Demir et al 1994;[29] Younes et al 1996[(41)]).

Also a high incidence of this abnormality is observed in placentas from babies of low birth weight.

Abnormalities of the Stroma:-

Stromal Fibrosis:-

More than 3% of Villi showing a marked increase in the stromal content of fibrous tissue is considered as abnormal[(42)]. Localized excess of stromal collagen is seen in villi rendered avascular by a fetal artery thrombosis and in the poorly vascularized villi immediately adjacent to an area of infarction.

Villous Edema:-

Macroscopically it appears bulky, friable and pale. Severe villous edema correlates inversely with umbilical arterial blood oxygen and pH values (Ilagan et al 1990)[43]

Villous edema occurs in some placentas from diabetic women, from cases of materno-fetal Rhesus incompatibility and from preeclampsia (Tarjan 1965)[(44)]. Quite marked oedema of villi is a feature of a number of placental infection eg-syphilis, toxoplasmosis, parvovirus, cytomegalovirus and often in placentas containing a large haemangioma, congenital nephrotic syndrome, fetal cardiac disorder, fetal anaemia, sacrococygeal teratoma, some fetal

chromosomal abnormalities, fetal metabolic disorders, maternal hyperthyroidism and hydatidiform mole.

Excessive number of Villous Hofbauer cells:

Villous Hofbauer cells are seen in abundance in young placentas and moderate numbers are seen in early third trimester placentas and in scattered villi in 80% of term placentas(Fox 1967b)[42]. In Mature placenta it is unusual to find Hofbauer cells in more than 2 -3% of Villi. Excess of Hofbauer cells are found in placentas from cases of maternal diabetes mellitus and fetal hydrops.

Abnormalities of Villous Vessels:- The terminal Villi of mature placenta usually contains 2-6 capillary vessels which are sinusoidally dilated .

Villous avascularity:

Major cause of this is fetal artery thrombosis. Avascular villi were noted in placentas from babies of low birth weight (Gruen Wald 1961)[45]

Villous Hypovascularity

It indicates that, the vessels seen in Villi are small & non-dilated. It is often secondary to an obstructive lesion of the fetal stem arteries like thrombus, an obliterative endarteritis, or a fibro muscular sclerosis. It is seen in placentas from prolonged pregnancies (Mulzer et al1970)[46]

Villous Hypervascularity

Terminal Villi containing an excessive number of vessels has been classed as "chorangiosis" by Altshuler (1984)[47]who considered that this abnormality could be diagnosed when microscopy with a X10 objective showed 10 Villi, each with 10 (or) more fetal vessels, in 10 (or) more non-infarcted areas of the placentas (Altshuler 1984)[47]. There is an absence of a continuous perivascular layer of muscle specific acting positive pericytes (Ogino & Redline 2000)[48]

Chorangiosis is strongly associated with perinatal death and congenital malformations and is considered as a response to low grade tissue hypoxia. (Altshuler 1991).(49) According to Ogino and Redline, chorangiosis is found in about 5% of pregnancies, most frequently in term placentas. They noted that chorangiosis may be associated with maternal DM, placentomegaly, delayed villous maturation and chronic villitis(Ogino and Redline 2000)[48]. Benirschke 1994[50] considers chorangiosis to be due to chronic fetal hypoxia; chorangiosis has also been reported in association with fetal anomalies (Balci et al 2001)[51] and in conjunction with a markedly raised maternal hcG concentration (Smith et al 2003)[52].

HISTOPATHOLOGY OF THE FETAL STEM ARTERIES:

Fibromuscular sclerosis:

This is characterized by a marked hyperplasia of the fibrous and muscular tissue of the media, with a proliferation of intimal fibrous tissue which grows into and eventually obliterates the vascular lumen. It occurs in

localized and generalized forms. The localized variety occurs under 3 circumstances.

a) In stem arteries supplying an area of villous infarction
b) In stem arteries supplying villi which are embedded in a fibrinous plaque
c) In stem arteries distal to an occluding thrombus.

The generalized form of fibromuscular sclerosis is found in placentas from stillbirths. The view that the vascular sclerosis is an antemortem lesion due either to placental inflammation (Fujikura & Benson 1964)[53] or to maternal infection (Becker and Dolling 1965)[54] is clearly indefensible, as is that maintaining it to be a manifestation of prolonged pregnancy (Dring and Kloos 1964)[55]

Obliterative Endarteritis:

It is characterized by an apparent swelling and proliferation of the intimal cells of the fetal stem arteries, with thickening of the subendothelial basement membrane.

Villous immaturity:

Immature (or) intermediate villi can be recognized by their relatively large diameter, small nondilated vessels, relative abundance of stroma, and uniform trophoblast which lacks both syncytial knots and vasculo-syncytial membranes. It occurs in term placenta in two forms. The first is small, isolated

group scattered amongst villi that are normally and fully mature, a pattern that is seen in 97% of placentas from full-term complicated pregnancies (Fox 1968 d)[56]. It is seen in centre of a fetal lobule & represents an index of persistent villous growth. In the second form most of the villi are markedly immature throughout pregnancy. There is a deficiency of terminal Villi and Immature intermediate Villi predominate. Becker[57] described it to be an asynchrony between the rates of placental and fetal maturation.

The condition which we classify as generalized villous immaturity is categorized by Kraus et al (2004)[58] as distal villous immaturity with placental over growth. Many placentas showing the pattern of delayed villous maturation are unduly large.

A delay in villous maturation occurs in placentas from diabetic women, materno-fetal rhesus incompatibility, pregnancies with fetal abnormalities including anencephaly, fetal aneuploidy such as trisomy 21, glutaric aciduria & occasionally uncomplicated pregnancies (Evers et al 2003)[59].

Accelerated villous maturation:

A completely mature villous pattern with a predominance of terminal Villi is found in a proportion of placentas from immature, prematurely delivered infants(becker1975)[57] and this form of feto-placental asynchronyis known as maturitas praecox placentae. Accelerated maturation has been described in placentas from women with pre eclampsia (schuhmaan, Geier1972)[60] and in IUGR. According to schumann (1975)[61] it is a compensatory mechanism to counter the effects of an inadequate uteroplacental blood flow.

Amnion nodosum

It may be due to desquamated skin or membrane injury.It is associated with fetal renal agenesis, oligohydramnios and pulmonary hypoplasia

Gross: It is seen as multiple superficial amniotic lesions, 0.2 to 0.4 cm in size, usually near insertion of umbilical cord.

Microscopic Appearance: Nodules of protuberant fibrinous material with entrapped squamous cells are seen.It is associated with stratified squamous metaplasia.

Umbilical cord pathology

Embryonic remnants

Allantoic duct [lumen is central between the artery], omphalomesenteric duct [epithelial lined lumen in cord lying subamniotically]

and embryonic vessels, together they are found in 23% of cases. Usually they are seen at fetal the end of umbilical cord.

Furcate insertion: Loss of covering of Wharton's jelly before insertion into chorionic plate.

Velamentous insertion

They are seen in 1% of placentas. They insert directly into the extraplacental membranes. The vessels split before entering into the placenta. They are associated with fetal blood loss (often massive), fetal distress. It is common in twins. It may cause massive fetal hemorrhage if located at the cervical opening.

Hematoma

It is significant if 4 cm long or more and 1.5 cm or more in diameter.It is associated with 2 vessel cord and decreased/absent fetal movement.

Knots : True knots: no clinical significance if they are loose and intrauterine fetal death occurs if it is tight

False knot: Occurs due to varicosity or lack of Wharton's jelly.It has no clinical significance.

Long cord (>100 cm) : It is associated with knots, entanglements, obstruction and thrombi. Prolapse of the cord may cause fetal distress/demise.

Short cord (<32 cm long) : It is associated with conditions of impaired fetal mobility including oligohydramnios, maternal uterine malformation, amniotic band syndrome, hematoma/hemorrhage and fetal anomalies of body wall

Thin cord (Diameter <1 cm): It is associated with tobacco use and oligohydramnios. Wrinkled and discoloured thin cord with 42 weeks gestational age is associated with deficient placental function and oligohydramnios.

Single umbilical artery:

Only two vessels (one artery and one vein) instead of usual two arteries and one vein are seen. Occurs in 1% of all cords. It is associated with congenital anomalies in 30%, involving heart, kidney, skeleton; also associated with small for gestation, prematurity, maternal diabetes, epilepsy, toxemia and twins (almost always present in acardiac twins).The single artery may be a persistent vitelline artery in cases of caudal regression and sironemelia.

Supernumerary vessels (4 or more vessels)

The additional vessels may be arteries or veins. It may be confused with embryonic nests and tangential artifacts. Cord length also increases with increasing fetal weight. Other factors associated with increased cord length include parity, the size of the uterine environment, increased fetal movement, male gender, and possibly genetics, as there may be an increased

risk of recurrent long umbilical cords in women with a past pregnancy with a long umbilical cord.

Decreased umbilical cord length is associated with decreased fetal movements from any cause dating from early in gestation, including Down syndrome, skeletal dysplasias, central nervous system lesions that impair fetal movement, amnion bands, and uterine structural malformations and multifetal gestation. The association of oligohydramnios with a shorter cord is inconsistent.

Umbilical cord coiling may serve to enhance cord hemodynamics, as arterial pulsations transmitted to the vein may help pump blood back up the cord from the placental capillary bed. Both abnormally straight (uncoiled) cords and excessively coiled cords are associated with an increased risk of adverse perinatal outcome. Risk factors for abnormal vascular coiling are extremes of maternal age for hypercoiling, obesity, gestational diabetes mellitus, and preeclampsia. An excessively long or coiled cord may be at increased risk for torsion.

Acute funisitis

It is a type of fetal inflammatory response to intrauterine infection.It is associated with heavy meconium staining and premature rupture of membranes.

The causes includes Listeria and Candida infections (cause abscesses and targetoid lesions in 25% of infected pregnant women), Actinomyces, HSV

(causes necrotizing funisitis) and syphilis. Higher incidence of major perinatal morbidity is seen in preterm vs. term placentas.

Microscopic Appearance: Neutrophilic infiltration of umbilical vein or arteries; necrosis of myocytes, meconium macrophages, mild neutrophilic inflammation. Mild-focal inflammation, moderate-diffuse inflammation, severe-necrotizing inflammation.

Necrotizing funisitis

- Stillbirth is common (31%).

Causes: syphilis (11%), HSV, Candida infections, prolonged rupture of membranes (62%), preterm labor. It is also associated with chronic villitis (58%) and acute chorioamnionitis (100%).Usually vein involvement occurs first.Fetal sepsis is rare.

Gross: barber-pole pattern of yellow-white bands between vessels and cord surface. In candida infections small focal yellow-gray necrotizing lesions are seen on the cord surface.

Microscopic Appearance: Perivascular concentric rings of inflammatory cells, necrotic cell debris, calcium deposits and neovascularization are seen. In chronic inflammation of the umbilical cord numerous mixed inflammatory cells forming ring-like bands around the umbilical vessels are seen.

Chorioamnionitis

It is usually caused by ascending infection of bacteria (fusobacterium in 18%, detected with Warthin-Starry stain), may cause premature rupture of membranes. Severe cases are associated with group B streptococcus infection. It is a major cause of fetal/neonatal infection, stillbirth, prematurity and perinatal morbidity and mortality. Prolonged (subacute) inflammation with amniotic necrosis is associated with chronic lung disease (bronchopulmonary dysplasia, Wilson-Mikity syndrome).It is associated with occult congenital syphilis in stillborn. More frequent and severe with younger gestational age.

Gross: Congestion of chorion and amnion is seen. Grey-yellow to grey-blue membranes is seen in severe or chronic chorioamnionitis and light green is suggestive of fusobacteria. Acute chorioamnionitis may be grossly normal.

Microscopic Appearance: Neutrophilic infiltrate of free membranes and those overlying chorionic plate occurs. Variable funisitis and septic intervillous thrombus may be seen. It is accompanied by mild to severe fetal vascular response in chorionic plate vessels.

Grading:

Extraplacental chorioamnionitis:

Mild-neutrophils in decidua only,moderate-neutrophils in chorion and subamniotic connective tissue, severe-necrotizing inflammation.

Chorioamnionitis:

Mild/stage 1-neutrophils in placental chorionic plate only, moderate/stage 2-neutrophils throughout chorionic plate and subamniotic connective tissue, severe/stage 3-necrotizing inflammation or multifocal abscesses.

Chronic chorioamnionitis:

It is the lymphocytic infiltration of chorioamnion. It is associated with chronic villitis of unknown etilogy (71%), maternal hypertension (20%), preterm infants (40%) and intrauterine growth retardation (15%).

Chronic intervillositis:

Histiocytic infiltrate in the intervillous spaces without villitis. It is associated with perinatal mortality and recurrent spontaneous abortion. It has an immunologic origin (IgM and complement deposits are seen in vascular lesions) and high recurrence rate (67%).

Microscopic Appearance: Prominent histiocytic infiltrate within intervillous spaces, villous fibrinoid deposits and atherosis are seen.

Massive Chronic Intervillositis

It is associated with malarial infection (18% of placentas with malarial parasites, predominantly primigravida women are associated with low birth weight. It is also associated with growth retardation and adverse pregnancy outcome.

Microscopic Appearance: Massive macrophagic inflammatory infiltrate in intervillous spaces with fibrin deposition, but no villous inflammation.

Villitis of unknown etiology

Chronic inflammatory cells within the stroma of chorionic villi, with no known cause. It is associated with intrauterine growth retardation (particularly in recurrences), stillbirth and prematurity.

METERIALS AND METHODS

Study Design

Prospective Study.

Study period

Two years from September 2009 to September 2011.

Study Place

Coimbatore Medical College and Hospital.

Sample size

50 placentas expelled during normal delivery or caesarean section.

Inclusion criteria

Live births with birth weight less than 2.5 Kg.

Exclusion criteria

Abortion, intrauterine death and still born.

Detailed history of the mother such as name, age, parity, address, occupation, marital history, previous obstetric history, past history of major illness, present medical history and habits were recorded on predesigned proforma with regard to the baby's gestational age. Birth weight and Apgar scores were observed from the record.

All placentas were collected immediately after delivery and washed in tap water which removed the blood collected in membranes and clots.

Grossing procedure

Placenta was examined in fresh state after delivery, handling the specimen with great care avoiding lacerations

Membranes:

Distance from the placental margin to the nearest point of rupture was measured. Membranes were examined for completeness, insertion, decidual necrosis, edema, extra-amniotic pregnancy, retromembranous hemorrhage, meconium staining, colour and transparency. A long 2-3cm wide section of membranes beginning with the point of rupture and extending to and including a small portion of placental margin were taken and rolled with amniotic surface inward, fixed for 24 hours and 3mm section was taken from the centre. Trim the remaining membranes from the placental margin

Umbilical cord:

The length of the cord and the shortest distance from the cord insertion to the placental margin were measured. Cord was examined for insertion, number of umbilical vessels, colour, true knots, torsion, stricture, hematoma and thrombosis. Cord was removed from the placenta 3cm proximal to the insertion, 2-4cm segment from its midpoint was taken, fixed for 24hours and 3mm section was taken.

Fetal surface:

Examination for colour, opacity, subchorionic fibrin, cysts, amnion nodosum, squamous metaplasia, thrombosis of fetal surface vessels and chorangioma was done.

Maternal surface:

Examination for completeness, normal fissures, laceration, depressed areas, retroplacental hemorrhage was done.

Measurement of the maximum diameter, thickness in the centre, weight (after trimming cord and membranes), and shape was noted.

With maternal side up on a flat surface, parallel sections were made with a large sharp knife at 10cm intervals. Four 2cm pieces were removed that included fetal surface and intact maternal surface, fixed for 24hours and 3mm sections were submitted for histology. One section included chorionic plate in an area with minimal subchorionic fibrin. Other section included the maternal surface.

Examination of all cross sections for infarcts (location, size, number), intervillous thrombi, perivillous fibrin deposition, pallor, consistency, calcification, cysts and tumors was done.

I. HAEMATOXYLIN AND EOSIN STAINING

Fixation – 10% Formalin

Technic – Paraffin section cut at 4 microns

SOLUTION PREPARATION

Haematoxylin - 10gram is dissolved in Absolute alcohol - 100ml with light heat. Aluminum Potassium sulphate 200 gram dissolved in 2 liters of warm distilled water. Both were mixed and boiled: 5 gms of mercuric oxide was added while boiling and cooled after two minutes. Prior to use, 3 ml of acetic acid for 100 ml of hematoxylin was added.

1% ACID ALCOHOL

70% alcohol - 990 ml.

Con.HCI - 10 ml.

EOSIN

Eosin - 10 gram D.H2O - 100 ml.	dissolved

Phloxine ‘B’ - 100 mg D.H2O - 20 ml	dissolved

Both were mixed and 780 ml of 90% alcohol was added. 4 ml of glacial cetic acid and saturated Lithium carbonate were added.

PROCEDURE

1. The slide was kept in xyline for 15 minutes.
2. It was washed in graded alcohol absolute 90% : 80% each 2 dips
3. Slide was washed in water for 5 minutes.
4. Stained in haematoxylin for 5 minutes.
5. It was washed in water for 5 minutes.
6. Differentiated in 1% acid alcohol 2 dips
7. Washed in water for 2 minutes.
8. Dipped twice in Lithium carbonate for blueing
9. Washed in water for 10 minutes
10. Dipped in 80% alcohol
11. Stained with eosin for 5 minutes.
12. Dehydrated in graded alcohol 80%, 90% then absolute alcohol
13. Cleared in xylene.
14. Mounted in D.P.X.

Result

Nuclei - Blue

Cytoplasm - Pink

III. PERIODIC ACID SCHIFFS REAGENT STAIN (PAS)

Fixation - 10% Formalin, Alcohol, Buffered Formalin.

Technique - Paraffin Section cut at 4 microns

SOLUTION PREPARATION

1% Periodic Acid

Periodic Acid - 1 gram

D.H2O - 100 cc

SCHIFFS REAGENT

In 100ml of warm distilled water 5 gram of Basic fuchsion is added and allowed to boil. It is then cooled and 10 gram of pattassium metabisulphite and 50ml of 1 Normal HCL 50ml are added and kept in dark place over night (24 hours) Then 25 gram of charcoal powder is added, shaken and kept in dark place for 2 hours. It is filtered and stored in refrigerator.

1. NORMAL HCL

HCL - 8.35ml

D.H2O - 91.65 ml

PROCEDURE

1. The slide is deparaffinised in 15 ml of xylene.
2. Washed in Graded alcohol ab.90%, 80% each 2 dips
3. Washed on H2O for 5
4. Placed in 1% periodic acid 5 minutes
5. Washed in H2O for 5
6. Placed in Schiffs reagent 15 minutes
7. Washed in H2O for 10
8. Stained in Haematoxylin for 3 minutes
9. Then washed in H2O for 2
10. Differentiated in 1% acid alcohol 3 dips
11. Washed in H2O for 2
12. Lithium carbonate 1 dip
13. Washed in H2O
14. Dehydrated (80%, 90%, Alcohol) cleared and mounted

Result

Glycogen, mucin, reticulin, Basement membranes, amyloid and other elements may show a positive reaction – rose to purplish red

Nuclei - Blue

Fungi - Red.

PAS WITH DIASTASE

Before step 4 saliva is put or 0.5% diastase for 45minutes. Then the PAS reaction is continued.

RESULT

Glycogen - Negative

PRINCIPLE

The Principle of the reaction is that periodic acid will bring about oxidative cleavage of the carbon bond in 1-2 Glycols or their amino or alkylamino derivative, to form dialdehydes. These aldehydes will react with fuchsin – Sulfurous acid which combines with Basic fucshin to form a magenta colour compound.

OBSERVATIONS AND RESULTS

TABLE – 1

PLACENTAS ACCORDING TO GESTATIONAL AGE

Categories	Total No. of Placentas	Percentage
Term pregnancies	24	48%
Preterm pregnancies	26	52%
Total	**50**	**100%**

CHART – I

PLACENTAS ACCORDING TO GESTATION AGE

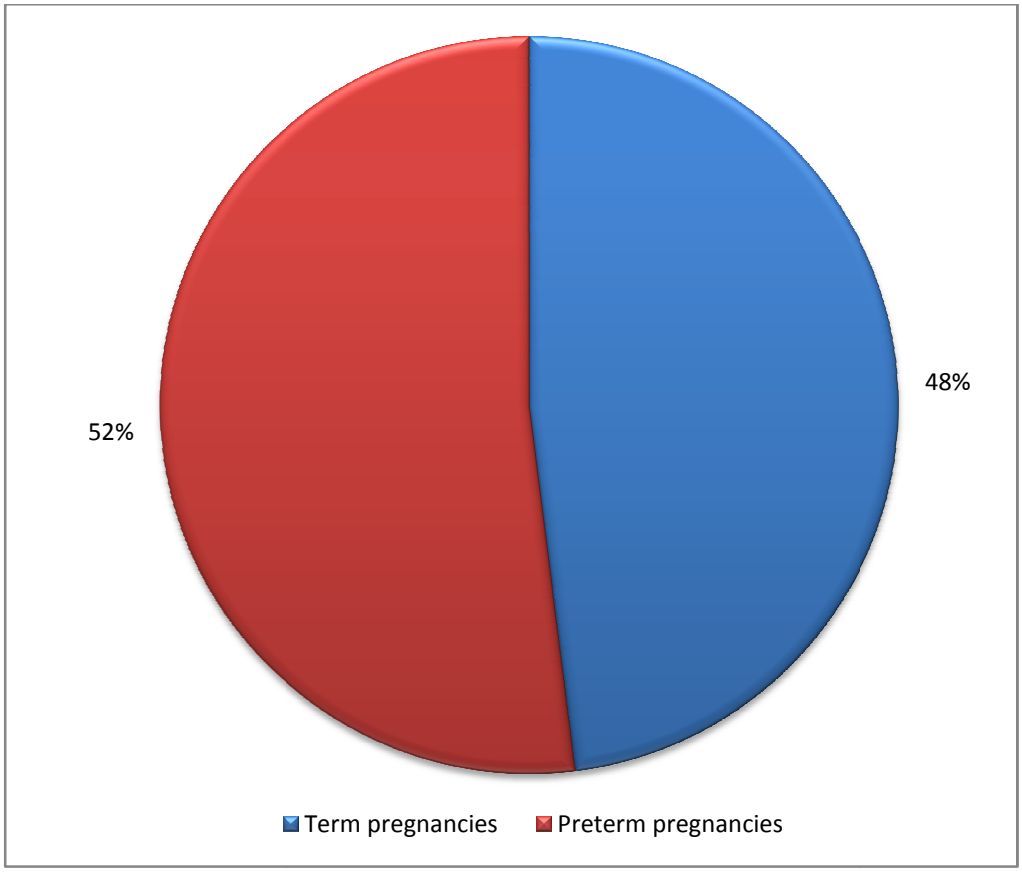


TABLE – 2

PLACENTAS ACCORDING TO HIGH RISK FACTORS

High Risk Factors	Total No. of Placentas	Percentage
Anemia	12	24%
PIH	11	22%
GDM	3	6%
Abruptio Placenta	1	2%
Rh negative	2	4%
Heart Disease	1	2%
Cervical Incompetence	1	2%
Twin gestation	1	2%
Oligohydramnios	6	12%
Uneventful	12	24%
Total	**50**	**100%**

CHART – 2

PLACENTAS ACCORDING TO RISK FACTORS

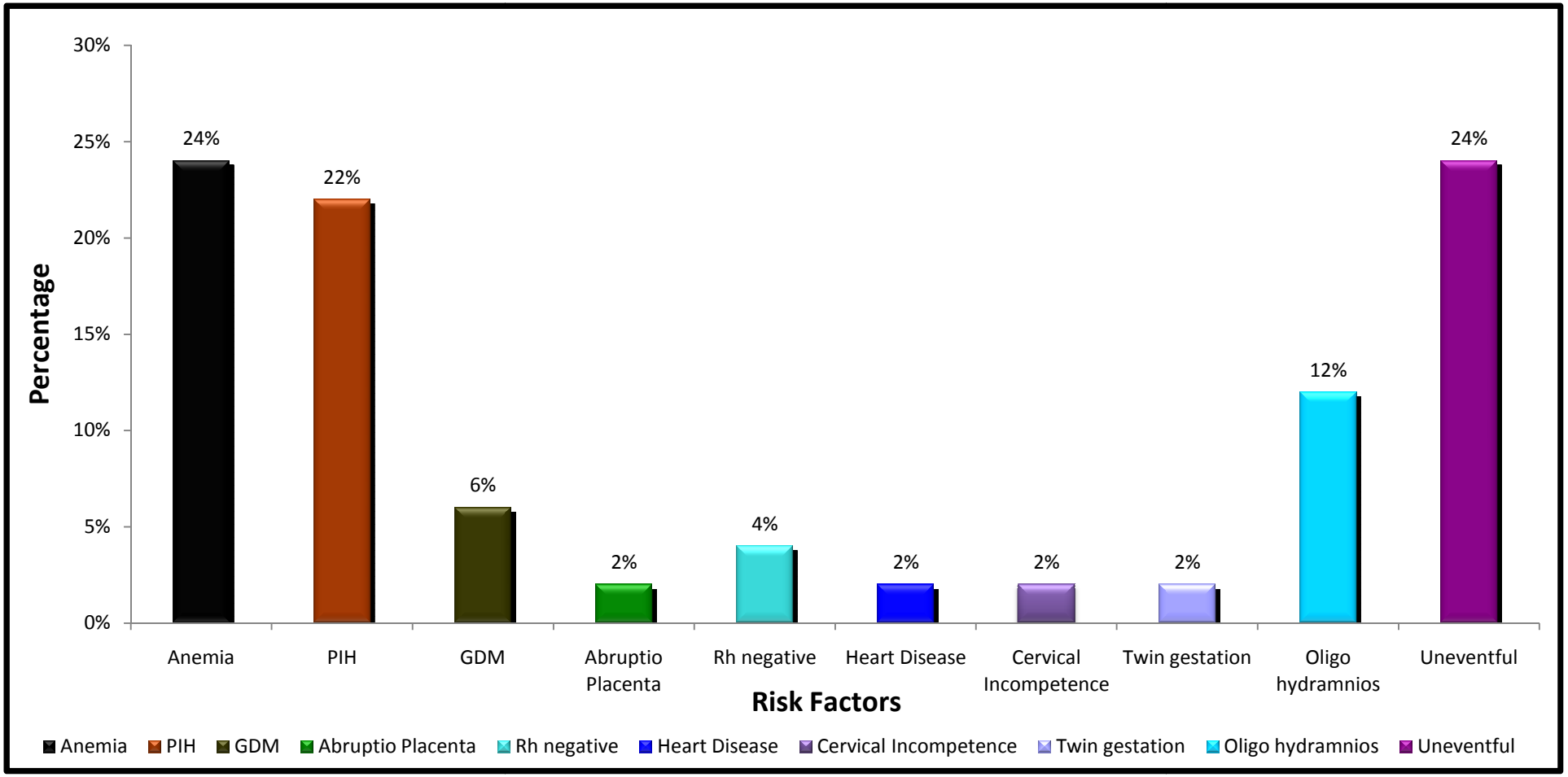


TABLE – 3

PERCENTAGE OF DELIVERIES ACCORDING TO BIRTH WEIGHT

Birth Weight	Total No. of Deliveries	Percentage
Low Birth Weight (1500 - 2499 gms)	25	50%
Very Low Birth Weight (1000 - 1499 gms)	24	48%
Extremely Low Birth Weight (<1000 gms)	1	2%
Total	**50**	**100%**

CHART – 3

PERCENTAGE OF DELIVERIES ACCORDING TO BIRTH WEIGHT

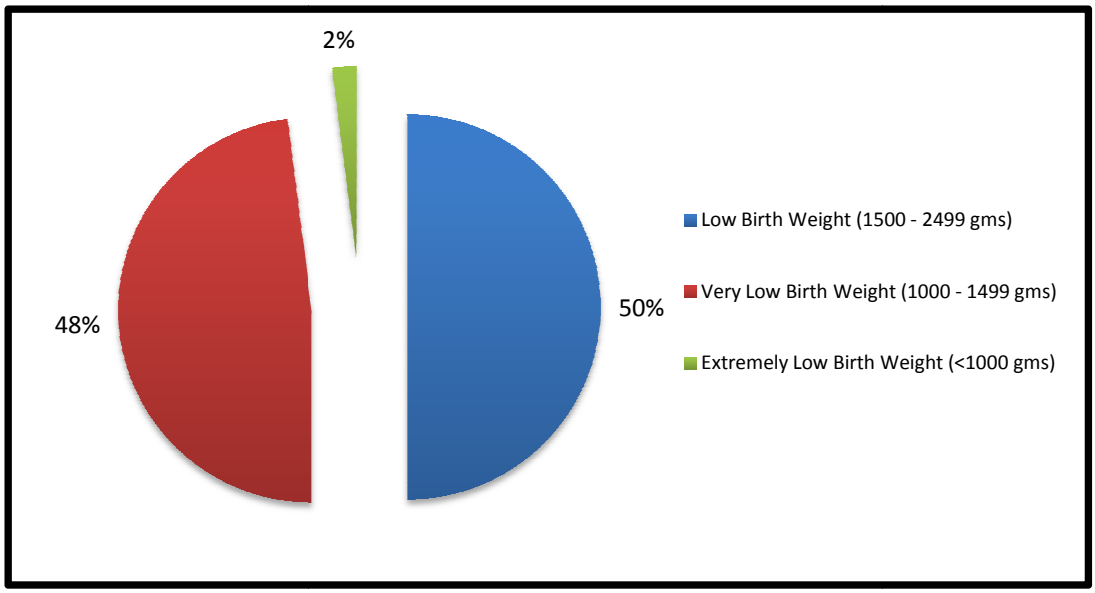


TABLE – 4

PLACENTAL WEIGHT AS COMPARED WITH GESTATIONAL AGE

Placental Weight	Term	Preterm
200-300 gms	4 (8%)	18 (36%)
301-400 gms	12 (24%)	8 (16%)
401-500 gms	8 (16%)	0
Total	**50 (100%)**	

CHART – 4

PLACENTAL WEIGHT AS COMPARED WITH GESTATIONAL AGE

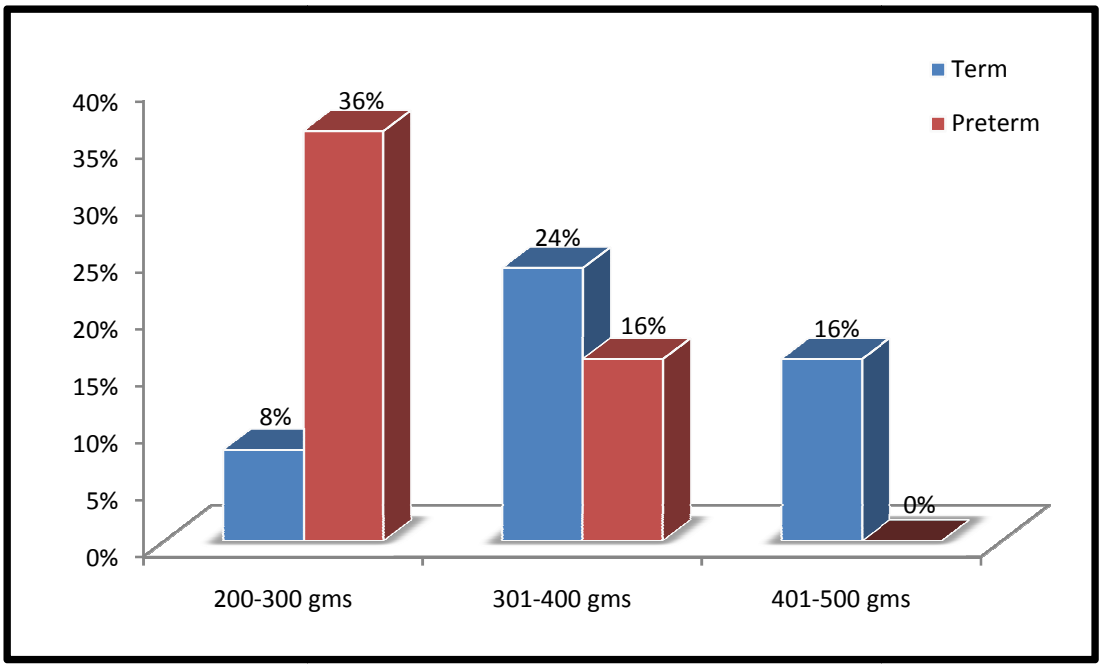


TABLE – 5

PLACENTAL WEIGHT IN HIGH RISK PREGNANCIES

Placental Weight	Anemia	PIH
200-300 gms	5	10
301-400 gms	4	1
401-500 gms	3	0
Total	**12**	**11**

CHART – 5

PLACENTAL WEIGHT IN HIGH RISK PREGNANCIES

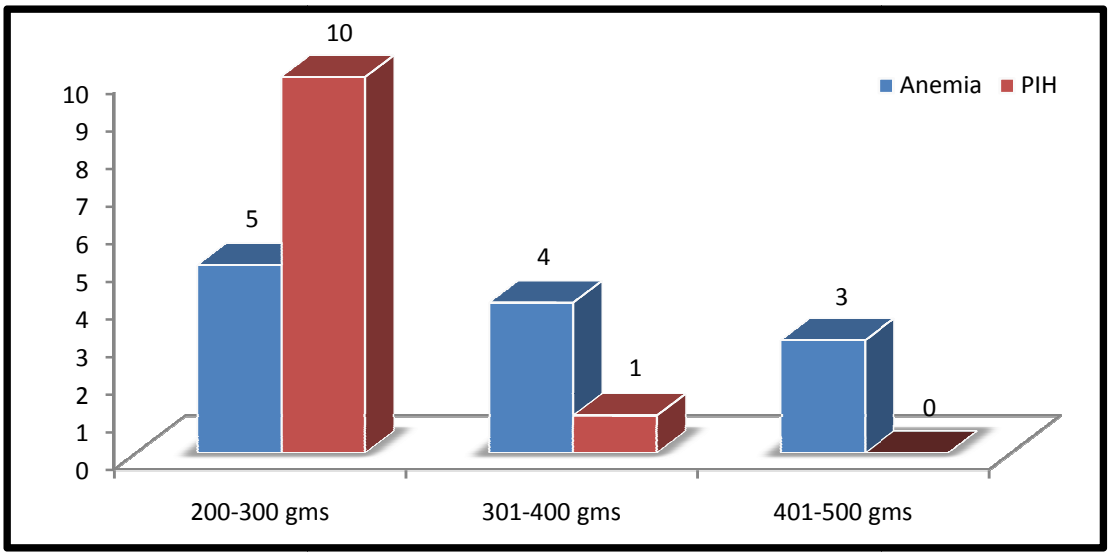


TABLE – 6

GROSS MORPHOLOGICAL CHANGES IN PLACENTA

Gross Morphological Changes	Total No.	Percentage
Placental infarct	14	28%
Perivillous fibrin	23	46%
Membrane opacities	24	48%
Calcifications	10	20%
Umbilical cord false knots	3	6%
Single umbilical artery	3	6%
Subchorial haematoma	2	4%
Retroplacental haematoma	1	2%
Circumvallate Placenta	1	2%
Accessory Lobe	1	2%

CHART – 6

GROSS MORPHOLOGICAL CHANGES IN PLACENTA

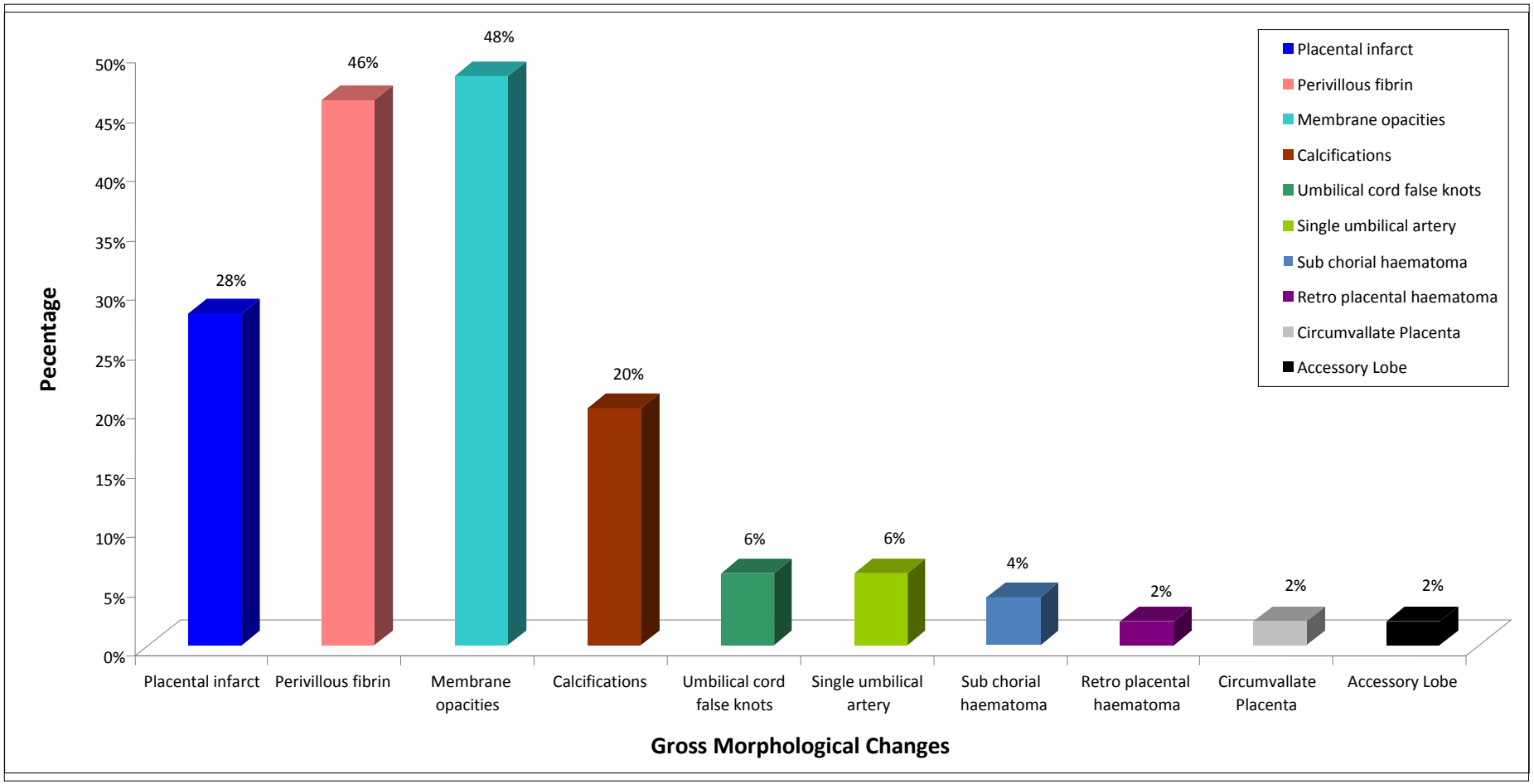


TABLE – 7

HISTOLOGICAL CHANGES IN PLACENTA

Histological Changes	Total No.	Percentage
Perivillous fibrin	23	46%
Infarct	14	28%
Calcifications	10	20%
Chorioamnionitis	24	48%
Increased syncytial knots	44	88%
Fibrinoid necrosis	44	88%
Increased Villous cytotrophoblast	33	66%
Basement membrane thickening	25	50%
Deficiency of Vasculosyncytial membrane	17	34%
Stromal fibrosis	16	32%
Villous hypovascularity	18	36%
Intravillous hemorrhage	25	50%
Distal villous hypoplasia	6	12%

CHART – 7

HISTOLOGICAL CHANGES IN PLACENTA

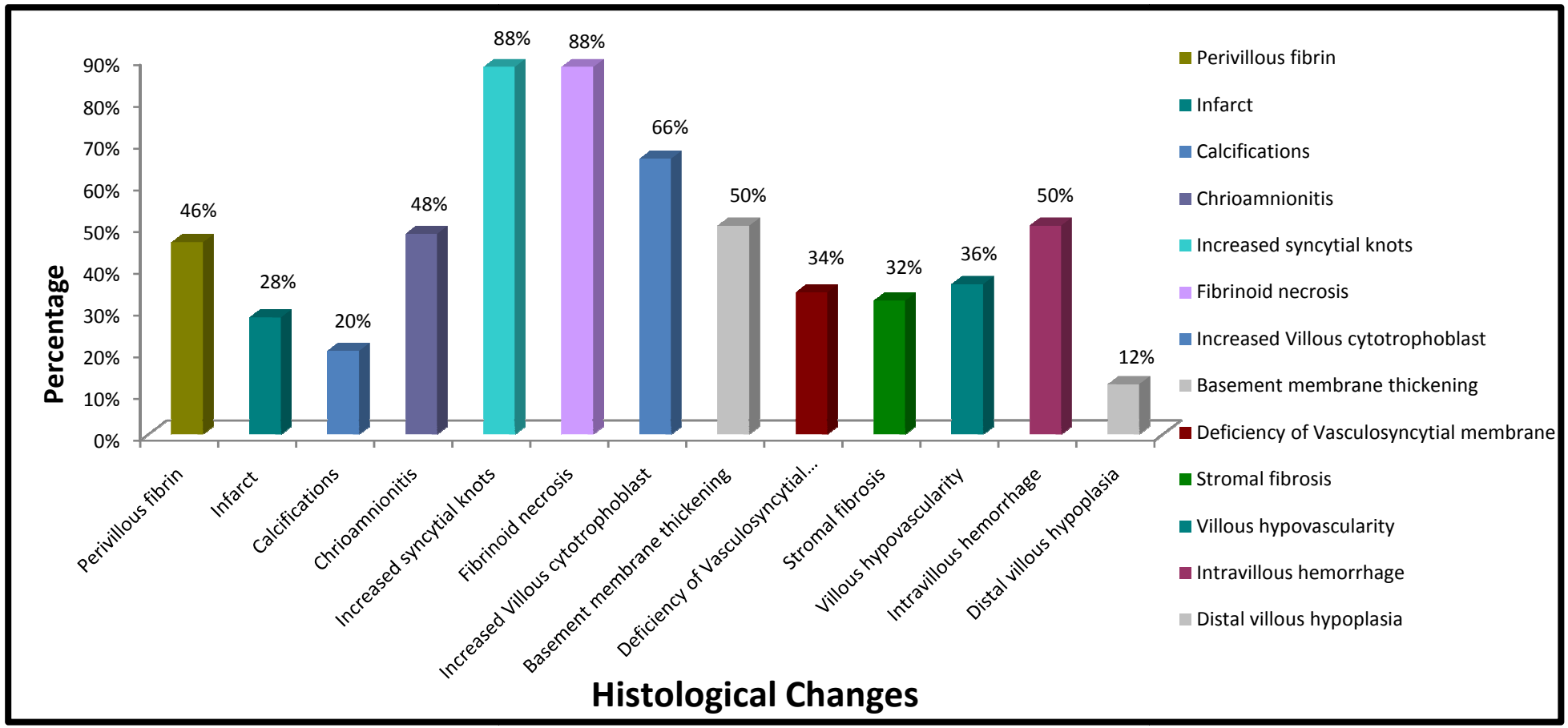


TABLE – 8

HISTOLOGICAL CHANGES IN ANEMIA COMPLICATING PREGNANCIES ACCORDING TO PLACENTAL WEIGHT

Histological Findings		PLACENTAL WEIGHT		
		200-299	300-399	400-500
		No. (%)	No. (%)	No. (%)
Syncytial Knots	>90%	1 (2%)	-	-
	>50%	4 (8%)	4 (8%)	3 (6%)
	30-50%	-	-	-
Fibrinoid Necrosis	>10%	2 (4%)	1 (2%)	-
	>3%	3 (6%)	2 (4%)	3 (6%)
	<3%	-	-	1 (2%)
Increased Vascularity		4 (8%)	1 (2%)	2 (4%)
Cytotrophoblastic Proliferation	<20%	-	2 (4%)	1 (2%)
	20-40	3 (6%)	2 (4%)	3 (6%)
	>40%	1 (2%)	-	-
Vasculosyncytial Membrane	<6	-	-	1 (2%)
	6-30	3 (6%)	3 (6%)	2 (4%)
	>30	1 (2%)	1 (2%)	1 (2%)
Basement Membrane Thickening	<3	3 (6%)	3 (6%)	3 (6%)
	>3	1 (2%)	1 (2%)	1 (2%)
Intervillous hemorrhage		4 (8%)	3 (6%)	3 (6%)

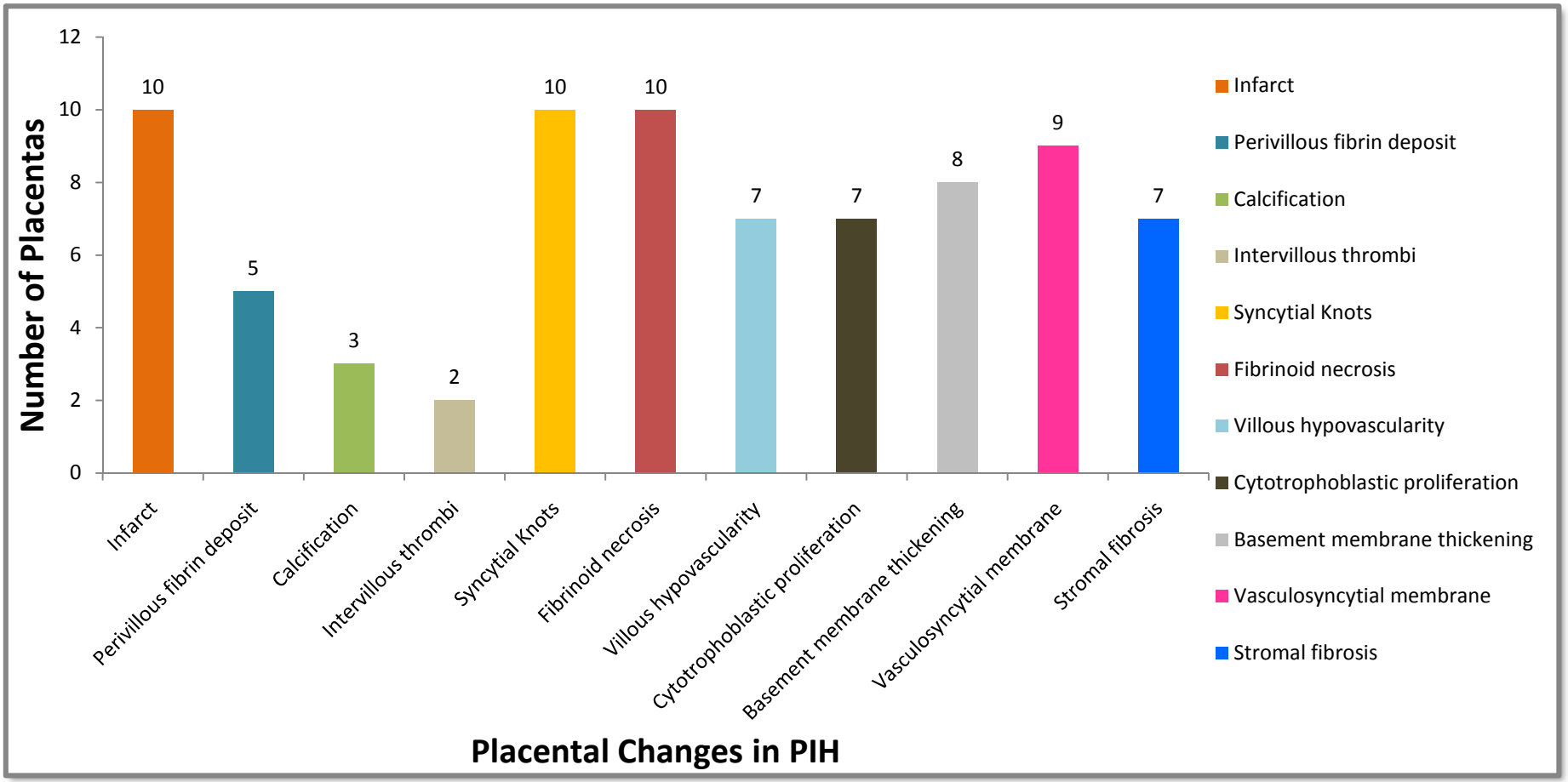
TABLE -9

PLACENTAL CHANGES IN PIH

Histological Changes	Numbers
Infarct	10
Perivillous fibrin deposit	5
Calcification	3
Intervillous thrombi	2
Syncytial Knots	10
Fibrinoid necrosis	10
Villous hypovascularity	7
Cytotrophoblastic proliferation	7
Basement membrane thickening	8
Vasculosyncytial membrane	9
Stromal fibrosis	7

CHART - 8

PLACENTAL CHANGES IN PIH



In this study, totally fifty placentas from low birth weight live births were collected, out of which 38 placentas were from high risk pregnancies and 12 placentas were from uneventful pregnancies.

In the total of 50 pregnant mothers, 24 had term delivery, other 26 had preterm delivery.

Out of the 50 low birth weight live births 25babies had weight range from 1500 g to 2499 g (low birth weight), 24 had birth weight between 1000 g-1499 g(very low birth weight)and one baby had birth weight of 950g (extremely low birth weight). All the collected placentas were subjected to pathological examination both macroscopically, microscopically and the results were documented and analysed.

Out of the 50 pregnancies 38 were high risk pregnancies among which 12 were due to anaemia, 11 were due to PIH and 3 were due to gestational diabetes mellitus. Rest of the high risk pregnancies included abruptio placenta, Rh incompatibility, heart disease, cervical incompetence, oligohydramnios and multiple gestation.

Grossly placental weight ranged from 200 g to 500 g.

The most commonly observed gross morphological changes were membrane opacities in 24 placentas followed by perivillous fibrin in 23 placentas. Placental infarct was observed in 14 numbers, calcification was noted in 5 placentas. umbilical

cord abnormalities was noted in 8 placentas, out of which 3 showed single umbilical artery,3 showed false knots, one had hematoma and the other was oedematous.

Fetal surface of placenta showed abnormalities in 5 cases out of which 2 showed subchorial hematoma, one showed accessory lobe and other showed retroplacental hematoma.

All the 50 placentas were subjected to histopathological examination and the most commonly identified finding was increased syncytial knots in 44 placentas and fibrinoid necrosis in 44 placentas. Chorioamnionitis was observed in 24 placentas and perivillous fibrin deposit was observed in 23 placentas. Other common findings were villous hypervascularity, increased villous cytotrophoblast, deficiency of vasculo syncytial membranes, basement membrane thickening, intervillous hemorrhage and calcification.

In this study, the histo-morphological changes in relation to placental weight were analyzed particularly in anemia and PIH. The placental weight was categorised into three (i.e., 200-299g, 300-399g, 400-500g) which correspond to the severity of the disease.

In anaemia complicating pregnancies the number of syncytial knots in the placenta kept increasing with the increase in the severity of anaemia. Fibrinoid necrosis kept increasing in proportion to the severity of anaemia. The cytotrophoblast proliferation (more than one layer of cytotrophoblast in a villi- >20%) was also found to increase in direct proportion to the severity of anaemia. The thickness of the

basement membrane of the villi trophoblast was found to be normal in placentas from uncomplicated deliveries whereas the thickness of the basement membrane was found to be increased in severe anaemia. The vascularity also increased in severe anaemia.

In PIH, the striking histological features were increased placental infarcts, syncytial knots and fibrinoid necrosis noted in ten out of eleven cases. Other observed findings were paucity of vasculo syncytial membrane in 9 cases, increase in basement membrane thickness in 8 cases, stromal fibrosis in 7 cases, PVF in 5 cases, calcification in 3 cases and intervillous thrombi in 2 cases. All the above mentioned results were analysed to arrive at a conclusion.

DISCUSSION

The placenta has been described as the mirror of the perinatal mortality. Intra uterine growth retardation is a complication of many pregnancies. The factors responsible for growth retardation include maternal malnutrition, anemia, preeclampsia, eclampsia, maternal infection, drug abuse, genetic factors, genetic diseases, congenital malformations, multiple gestations, placental/cord abnormalities and maternal smoking .Miscellaneous causes like short interpregnancy interval, race, maternal age and low socio economic status also contribute to small for gestational age babies.

In many cases, the specific causes were never identified. Growth and survival of the fetus is essentially dependant on development, formation, maturation and function of the placenta. Hence, a study of the morphology of the placenta is very important and useful in learning its relationship and its predictive value to fetal weight and possible birth defects.

Earlier, workers attended to the morphology and morphometry of placenta in relation to the baby's weight in term and preterm deliveries. In normal preterm and term infants there is a direct relation between birth weight and weight of the placenta.

This study mainly deals with both gross and histopathological changes that occurred in low birth weight live births. The placental parameters like weight and size in normal term and preterm babies were measured. It was found that the weight and size of the placenta were significantly less than normal in preterm and term low

birth weight deliveries. Out of the 50 placentas, 26 were from preterm deliveries. Among 26 preterm placentas, 18 were weighing less than 300 grams. This finding is comparable with R.D.Virupaxi et al[(62)]. In high risk pregnancies like anemia and PIH the placental weight is significantly reduced with the severity of the diseases[(63)] .

In this study the average mean weight of placenta in low birth weight live births was 300 grams. Mallik et al[(64)] have reported 5 cases of toxemia with the placental weight less than 300 grams.

Nobis and Dass [(65)] in their study have shown that the placental weight in toxemic cases varies from 279 to 407 grams.

Bhartia et al [(66)], have shown reduced placental weight in severe toxemia, the lowest weight recorded being 280 grams.

Placenta from eclampsia is small in size when compared to the normal placenta. In the present study 40 placentas (80%) had normal discoid shape which had no significance in low birth weight placentas. One placenta had accessory lobe being 2% in the present study.

Umbilical cord attachment is a specialized anatomy of the placenta and fetus[(67)]**.** The commonest mode in insertion of the umbilical cord was peripheral in 56% of cases followed by central in 44% of cases. Velamentous, battle dore, furcate insertion were not observed in the present study. This observation is not comparable with the study done by Naramshima and Vasu Deva et al in which central insertion

was common. But in another study done by R.D.Viruppaxi et al[62]. The umbilical cord insertion was more towards the margin with the increase in severity of anemia. In the present study peripheral insertion of the umbilical cord was seen in 10 cases of anemia complicating pregnancies.

False knots were noted in 3 cases (6%) and thrombosis noted in 1 case (2%) in this study. False knot had no clinical significance but thrombosis of the cord was associated with severe preeclampsia [63].

Another interesting observation in the present study was Single umbilical artery(SUA). Many observations have been published about this umbilical cord maldevelopment which was seen in 7% twin gestations and 1% of term pregnancies[68,69]. SUA is common in twins, diabetic pregnancies, in association with long cords and small placentas. In the present study, there were 3 SUA placentas, two of which were associated with twin gestation and one with GDM.

Chorioamnionitis which prevailed among SGA new borns may occur as a consequence of the penetration of the micro organisms from the vaginal canal (Ascending infection): This is the most common cause of chorioamnionitis in human beings[70]. The association between chorioamnionitis and fetal growth restraint is well established. In this study, grossly membrane opacities were seen in 24 placentas (48%). Corresponding histopathological changes were consistent with chorioamnionitis.

Placental infarction of >5% surface area is considered pathological and more frequently seen in toxemia and IUGR due to thrombotic occlusion of maternal utero placental vessels [(71)]. Intra uterine hypoxia leads to coagulation necrosis of the villus tissue, secondary to the occlusion of the placental vessels in cases of improper vascular adaptations during placentation[(72)]. Studies performed with doppler flow meter in cases of IUGR have shown a decrease in uterine placental blood flow, associated with an increase of vascular resistance as a cause of chronic hypoxia and IUGR [(73-75)].

Among the 50 placentas, placental infarcts were observed in 14 cases (28%). This is almost comparable with the study done by Mirchandhini et al [(76)]. Out of the 14 cases 10 were from PIH. This correlates with the study done by Aparna Narasimha et al [(63)] and R.D.Virupaxi et al [(62)].

Extensive peri villous deposits (PVF) has been associated with a decrease of blood flow in the intervillous space and has been frequently associated with the presence of placental infarction[(77)]. In the present study, 23 cases (46%) of PVF deposits were observed. Of the 23 cases, most were associated with IUGR and PIH. This is comparable with the study done by Aparna Narasimha et al [(63)].

In general, calcification is regarded as placental senescense or degeneration[(78)]. The incidence of calcification of the placenta in the present study was 20%. This was most commonly associated with preeclampsia and IUGR. This is almost agreeable with the study done by R.D.Virupaxi in which 22% of cases showed calcification which were associated with PIH [(63)].

The incidence of retroplacental hematoma was 2%. This case was associated with abruptio placenta. The incidence of retroplacental hematoma was 11.1% in another study which was associated with PIH[(63)]. But in the present study, abruption was not associated with PIH.

Sub chorionic thrombosis was seen in 2 placenta. One case of IUGR have been reported in associated with massive subchorial thrombosis [(71)].

Syncytial knots are seen with increased frequency in the last weeks of pregnancy and more villi show these changes in high risk pregnancies[(64&76)]. It is an indication of excessive aging due to either post maturity or a disease state causing placental insufficiency.

Increased syncytial knots were noted from placentas of anaemia,PIH, GDM complicating pregnancy and from materno fetal Rh incompatibility. Out of 50 placentas, 44 showed increased number of syncytial knots (88%) in the present study. It is comparable with all other similar studies in literature[(64&76)] **.** In anemia complicating pregnancy in almost all cases, an increased number of syncytial knots were found.In PIH, 90% of placentas showed increased number of syncytial knots. In a similar study by Aparna Narasimha et al an increased frequency of syncytial knots (90.47%) was seen [(63)]. The above mentioned results clearly indicates that syncytial knot formation is a feature of high risk pregnancies. It directly correlates with the incidence of IUGR.

Fibrinoid necrosis is nothing but a fibrinoid patch that replaces villous stroma and the vasculature underneath a more or less intact trophoblastic cover. It occurs occasionally in normal mature placentas, but the incidence is increased in complicated pregnancies. Significant villous fibrinoid necrosis was noted in 44 cases (88%) in the placentas of PIH, anemia and IUGR. These findings are in concordance with other studies[63&71].

Cytotrophoblasts (more than 2 cells per peripheral villous cross sections >20%) are usual findings in immature placentas. They also exist in persisting immaturity, erythroblastosis, maternal anemia and maternal diabetes mellitus. In the present study, 66% of placentas had high villous amount of these cells, the rise in counts accompanied the severity of the maternal anemia, PIH and GDM. But in a similar study by Aparna et al, 86% of the placenta had increased cytotrophoblast.

The incidence of villi showing a thickened Basement Membrane in more than 3% of the villous population is regarded as abnormal and is a common feature of placentas from toxemia, IUGR and GDM. In the present study, 25 placentas showed increased basement membrane thickness (50%). Mostly all these were associated with PIH, IUGR and GDM. These findings concurred with those of other authors ***(79&80)***.

In the present study, 32% of placentas showed stromal fibrosis. There was an increased incidence of fibrotic placenta in pregnancy complicated by PIH. Another similar study by Fox et al, also correlated with this finding[81] .

Vasculo syncyntial membrane (VSM) is an index of fetal hypoxia. The incidence of VSM deficiency was noted in 34% of cases. The paucity of VSM was seen in higher grades of PIH, correlating with the severity of disease. It is also seen in maternal anemia and maternal heart failure.

Chorangioma is an expansile nodular lesion composed of capillary vascular channels, intervening stromal cells and surrounding trophoblast. Intermediate sized chorangioma are associated with IUGR [(82)]. In the present study, one case of chorangioma was found.

Placentas with Distal villous hypoplasia are extremely small for gestational age. The feto placental weight ratio is generally very high and other manifestations of maternal under perfusion like infarction, abruption and changes consistent with severe oligo hydramnios are common. This pathological pattern confirms closely to the clinical entity characterised by severe fetal growth retardation and abnormal pulsed flow doppler studies which has a prevalence of approximately 10% in a selected series of high risk pregnancies[(83)]**.** In the present study, 6 cases accounting for 12% were seen with similar findings.

SUMMARY

- PIH and anemia are the most common conditions that produce low placental weights and low birth weight (LBW) live births.
- Placental morphological changes increase in direct proportion to the severity of diseases.
- Membrane opacities (48%), perivillous fibrin (46%) and placental infarcts are the most commonly observed morphological changes in LBW live births.
- Single umbilical artery is associated with congenital anomalies of the babies.
- Syncytial knots (88%) and fibrinoid necrosis (88%) are the most common histological finding in LBW live births.
- Increased syncytial knot formation is a consistent feature of anemia and PIH.
- Increased basement membrane thickness is a common finding in severe anemia.
- Increasing number of placental infarcts are the specific finding in all PIH.

CONCLUSION

In general, both gross and histological changes of the placenta were more in high risk pregnancies. The commonly observed high risk categories were anemia, PIH, diabetes, oligohydramnios, Rh incompatibility, cervical incompetence and heart disease complicating pregnancies. 76 % of pregnancies were high risk in the present study. Out of these, 24% were anemia complicating pregnancy, 22% were PIH, 12% were oligohydramnios and 6% were diabetes complicating pregnancy.

Among the gross placental changes, membrane opacities (48%), perivillous fibrin (46%) and placental infarcts (28%) were the most commonly observed changes. These types of changes were mostly associated with PIH and anemia complicating pregnancy. Calcification was noted in 20% of the placentas. Though it is a normal finding in term placentas, in the present study it is especially associated with villous necrosis.

Three placentas with single umbilical artery were observed and out of the three, two babies had renal anomalies.

Most commonly observed histological changes in the low birth weight live births were increased syncytial knots (88%) and fibrinoid necrosis (88%). Other less common findings were chorioamnionitis (48%), perivillous fibrin deposits (46%), deficient vasculo syncytial membrane and increased villous cytotrophoblast.

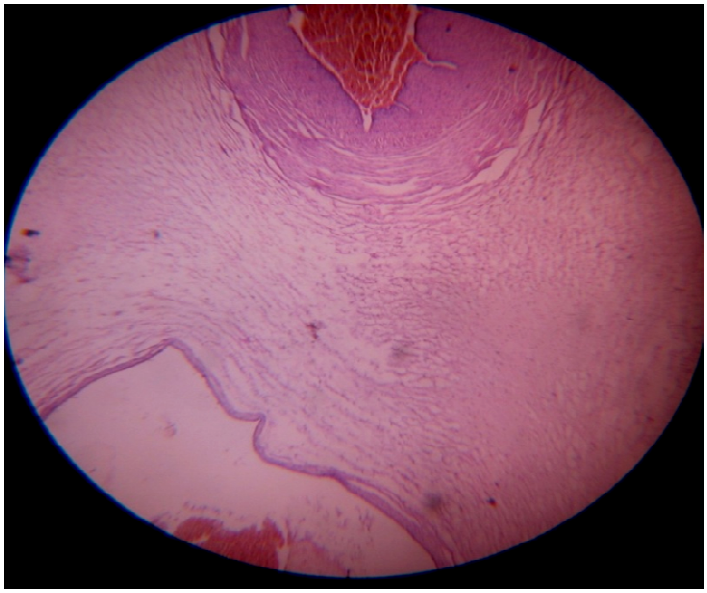
Increased syncytial knot formation was a consistent feature of anemia and PIH. Increased basement membrane thickness was noted in wherever the severity of anemia is more.

Increased placental infarct is a specific finding in PIH complicating placentas. Membrane opacities were the most common finding in chorioamnionitis.

Figure No – 1
Single Umbilical Artery

Gross picture showing two umbilical vessels

Figure No – 2
Single Umbilical Artery



Low power view showing single umbilical artery and vein

Figure No – 3
False Knot

Gross picture showing a false knot in umbilical cord

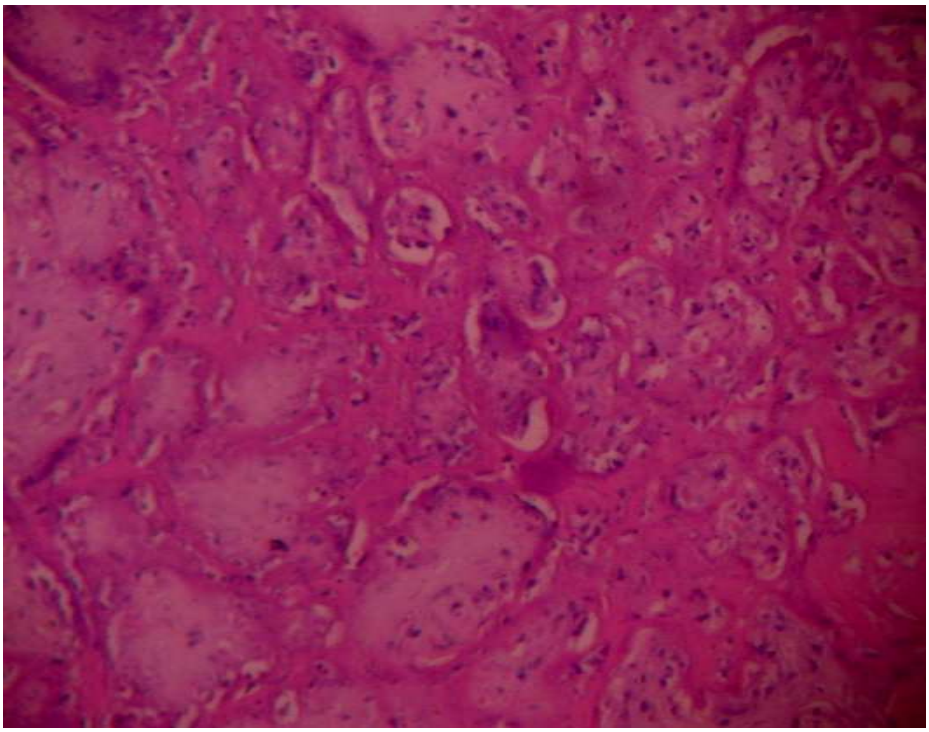
Figure No – 4
Circumvallate Placenta

Gross picture showing a circumvallate placenta viewed from the fetal aspect

Figure No – 5
Perivillous Fibrin Deposit

Gross picture showing the Plaque of perivillous fibrin - irregular in outline and whitish yellow in colour

Figure No – 6
Perivillous Fibrin Deposit

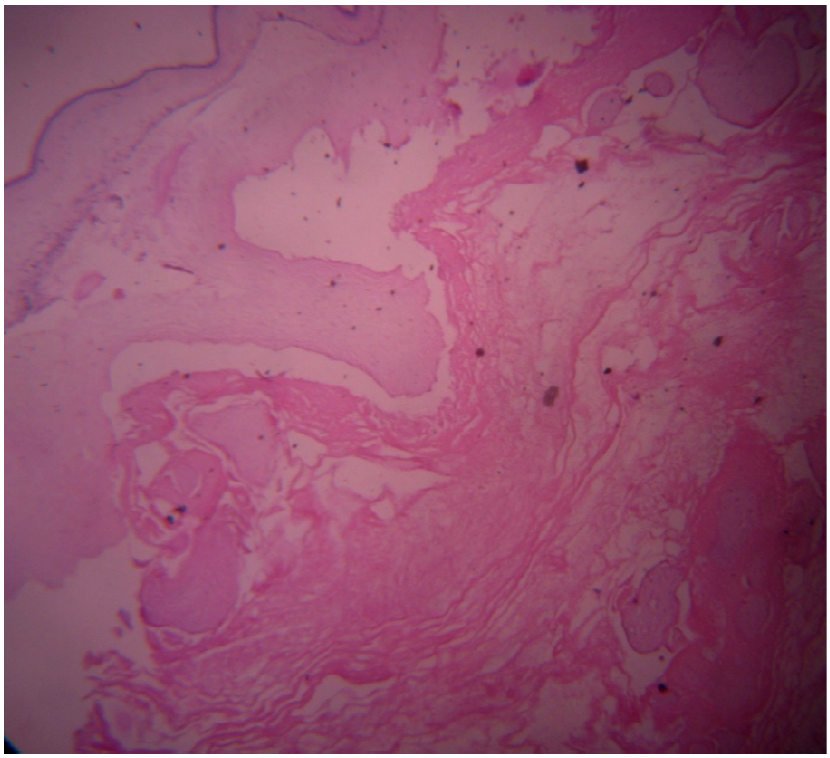


Microscopy – The villi are widely separated from each other by fibrin which is filling in and obliterating the intervillous space.

Figure No – 7
Subchorionic Thrombi

Gross picture showing massive thrombi indenting the placental parenchyma

Figure No – 8
Subchorionic Thrombi

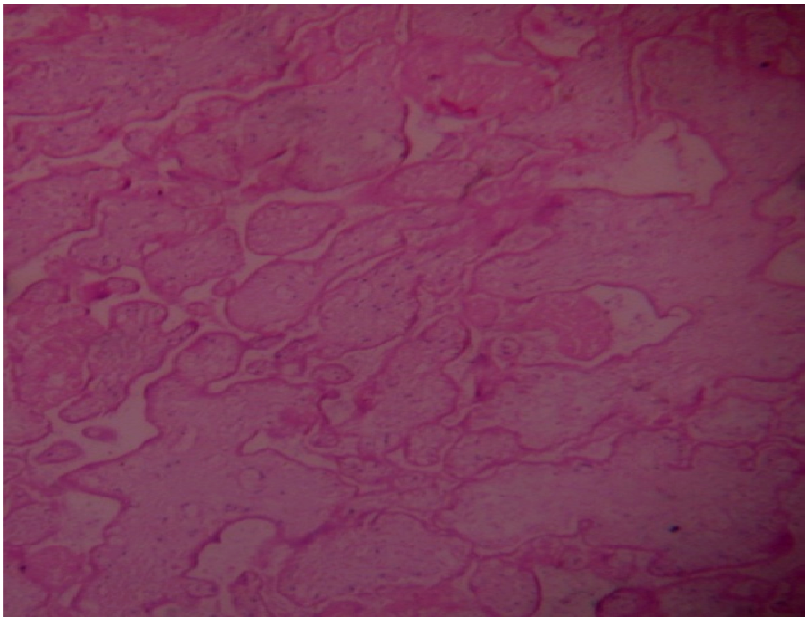


Microscopy showing degenerated laminated fibrin thrombi

Figure No – 9
Old Placental Infarct

Gross picture showing an old placental infarct

Figure No – 10
Old Placental Infarct



Microscopy showing the ghost like appearance of villi in an old placental infarct. The villous trophoblast has undergone complete necrosis and represented by a perivillous rim of acidophilic material (H & E)

Figure No – 11
Accessory Lobe

Gross picture showing an accessory lobe connected to the main placental mass by a narrow isthmus of chorionic tissue.

Figure No – 12
Peripheral Insertion of Umbilical Cord

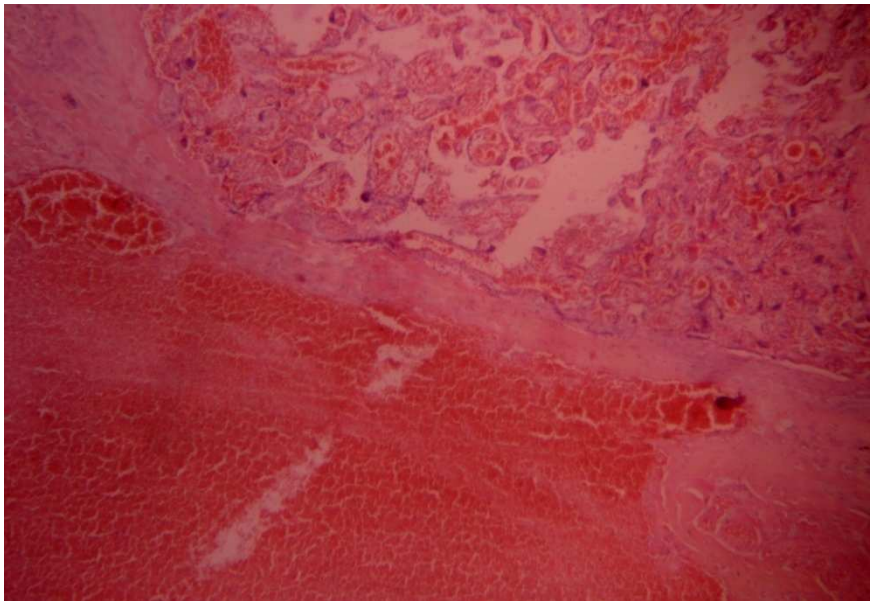
Gross picture showing the umbilical cord insertion eccentrically into the placental disc.

Figure No – 13
Abruptio Placenta

\

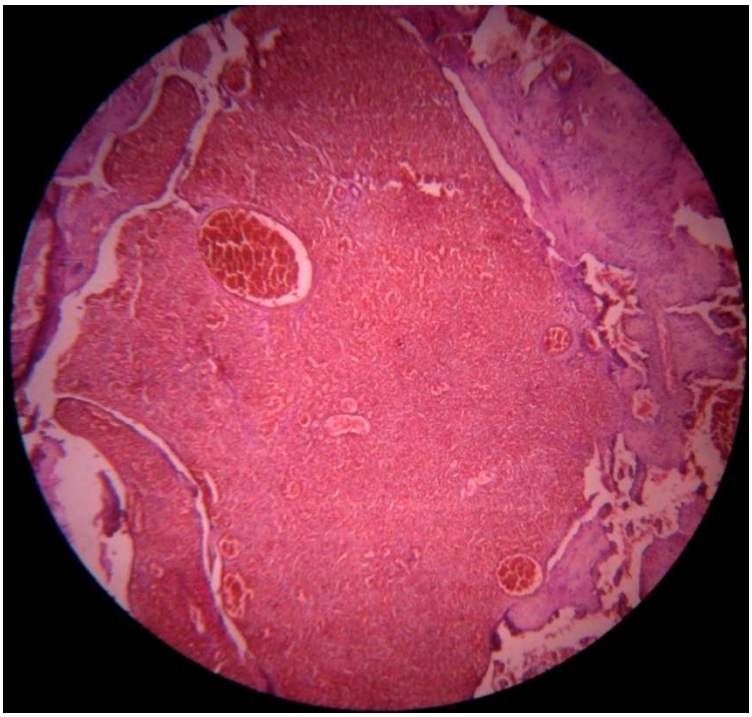
Gross picture showing retroplacental haematoma intending the placental parenchyma

Figure No – 14
Abruptio Placenta



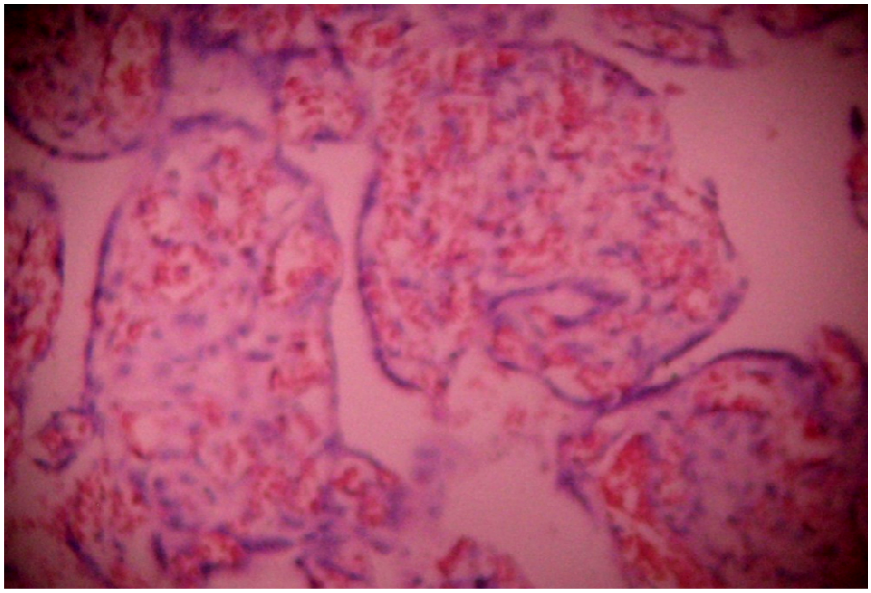
Microscopic picture showing retro placental haematoma – the overlying the basal plate and villi are not infarcted

Figure No – 15
Chorangioma



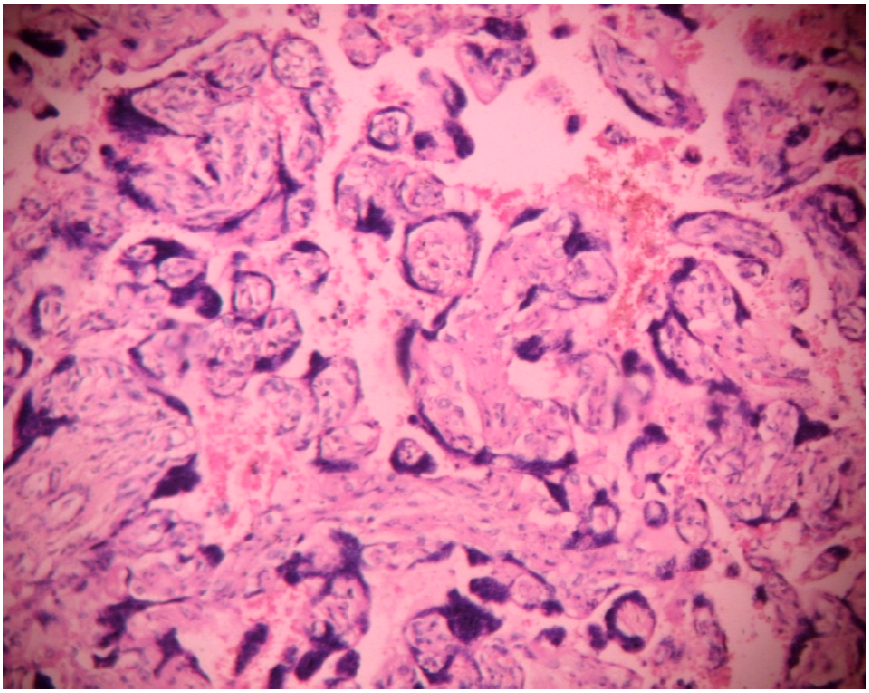
Microscopic picture showing capillary type of Chorangioma

Figure No – 16
Chorangiosis



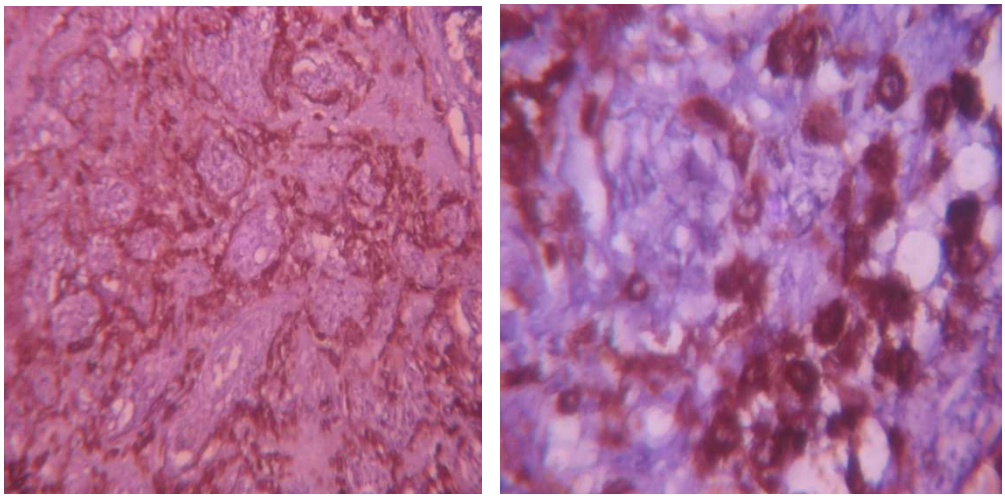
Microscopic picture showing more then 10 capillary per terminal villi cross section

Figure No – 17
Increased Syncytial Knots



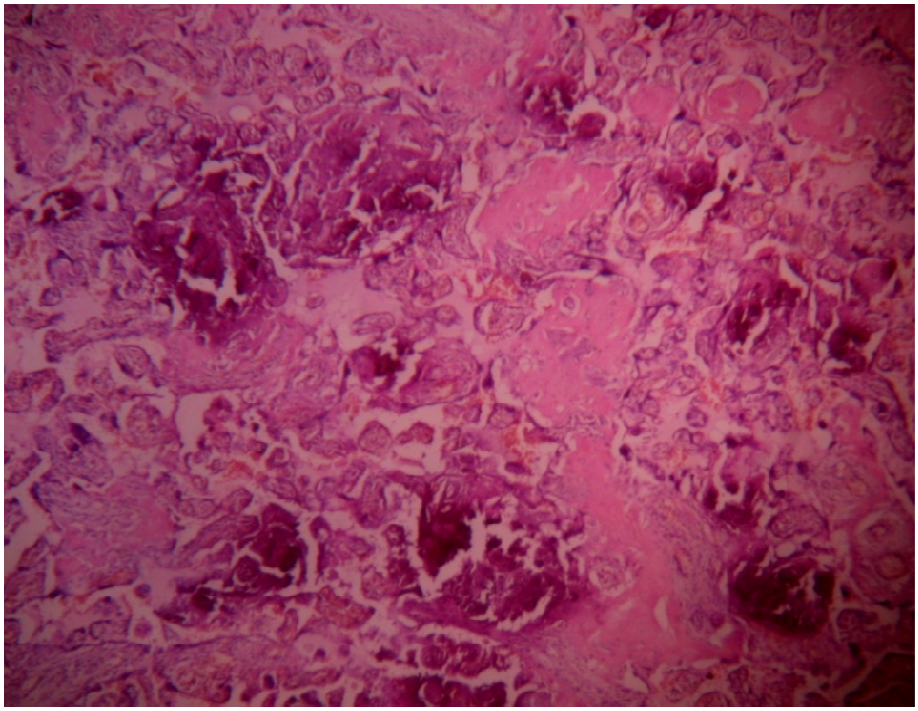
Microscopic picture showing increased syncytial knots (Tenny – Parker effect)

Figure No – 18



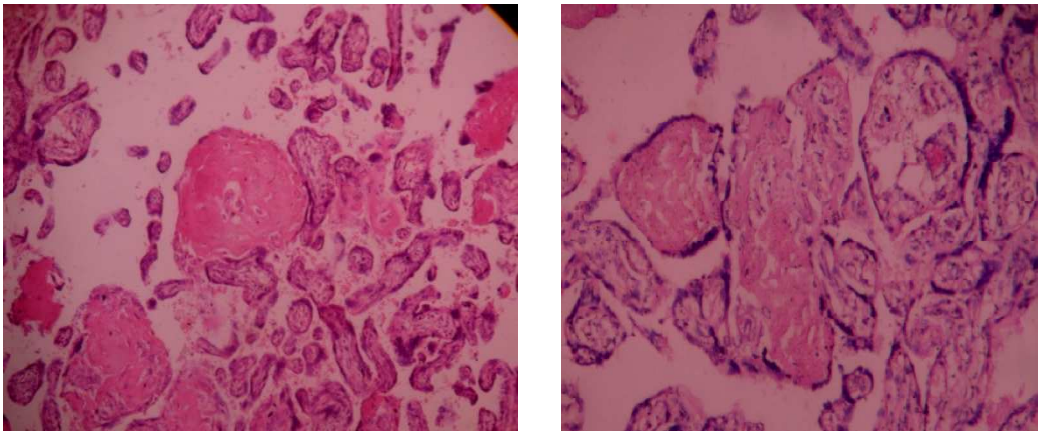
Microscopic picture showing AE 1/AE3 (Cocktail) Cytoplasmic positivity of cytotrophoblast (IHC)

Figure No – 19
Calcification



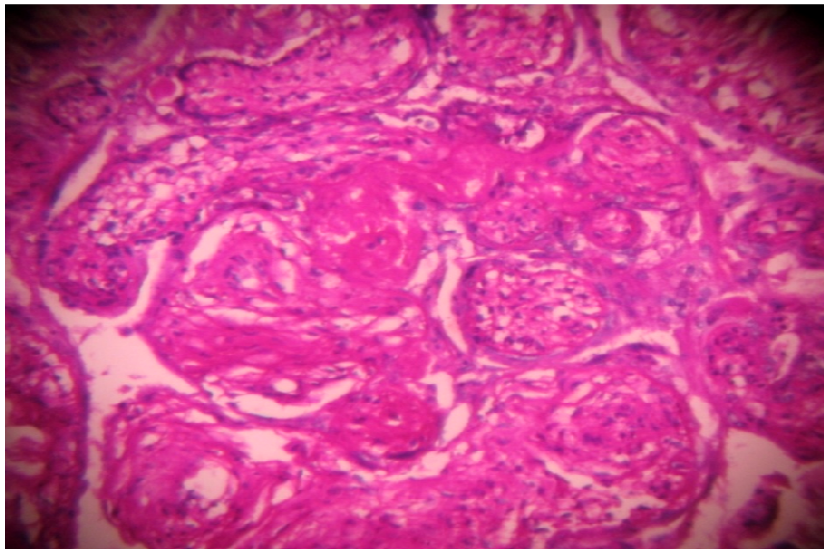
Microscopic picture showing the calcification of villous structure

Figure No – 20
Fibriniod Necrosis



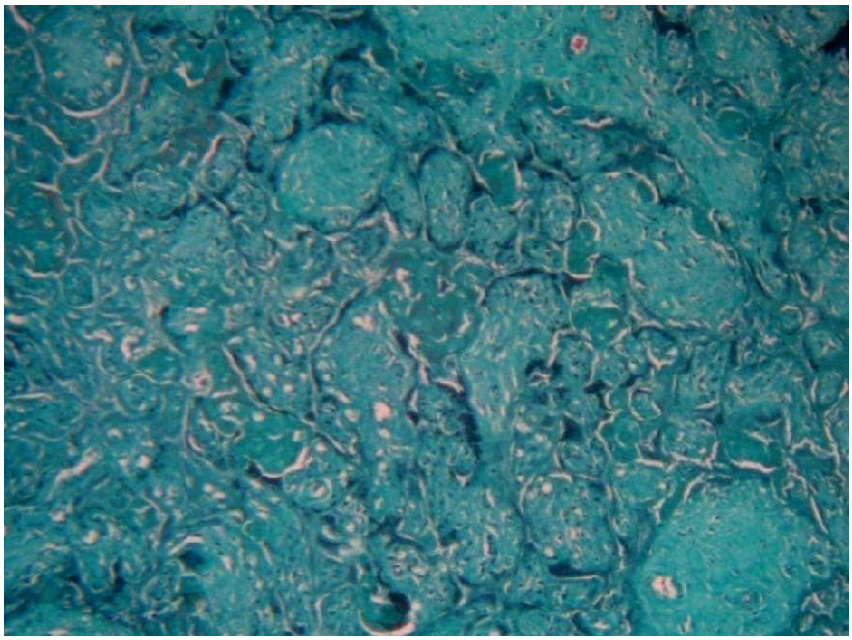
Microscopic picture showing villi which has undergone complete fibrinoid necrosis

Figure No – 21
Basement membrane thickening



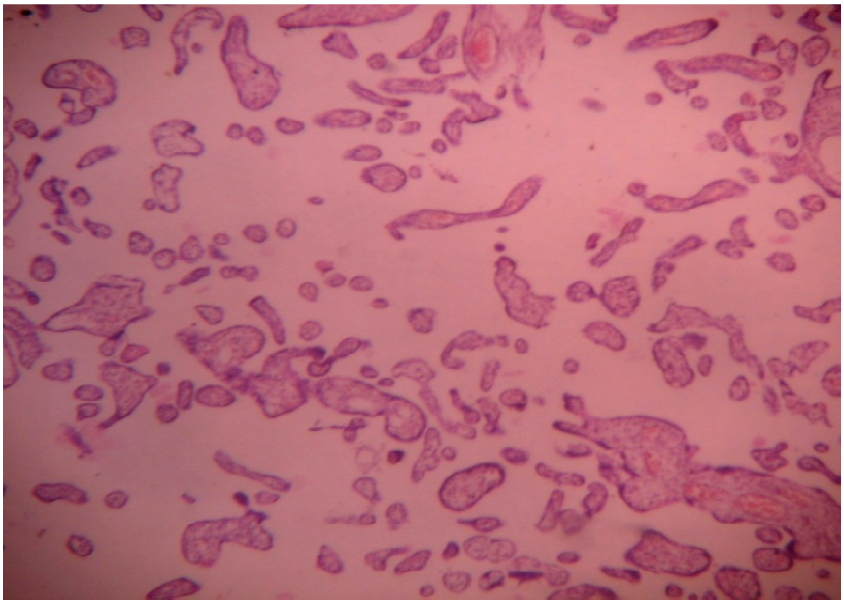
Microscopic picture showing thickened basement membrane (PAS Staining)

Figure No – 22
Avascular villi



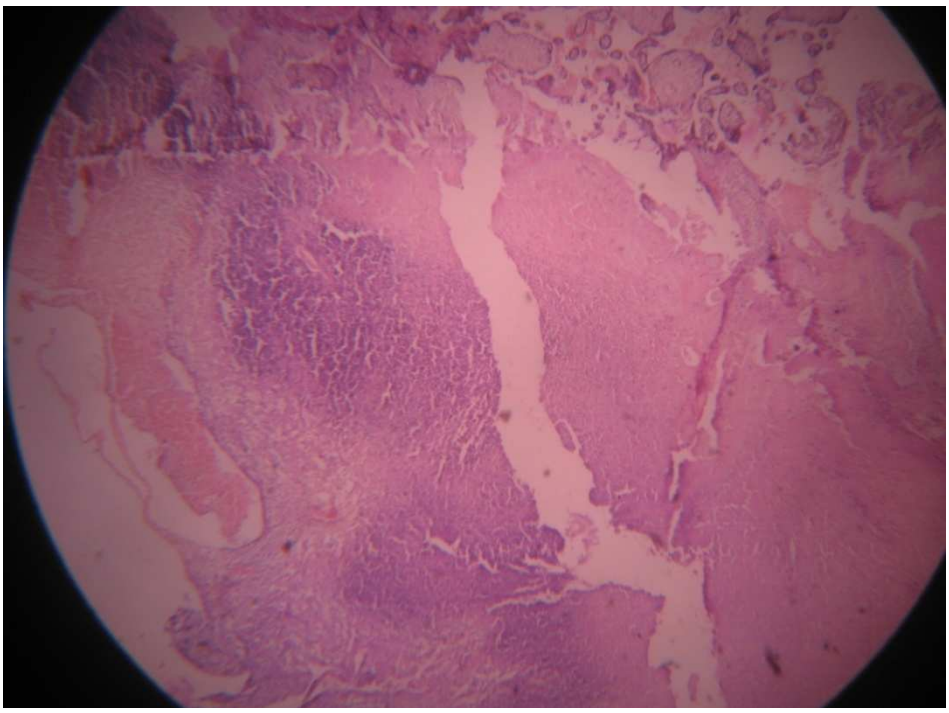
Microscopic picture showing fibrotic avascular villi (masson trichrome stain)

Figure No – 23
Distal Villous Hypoplasia



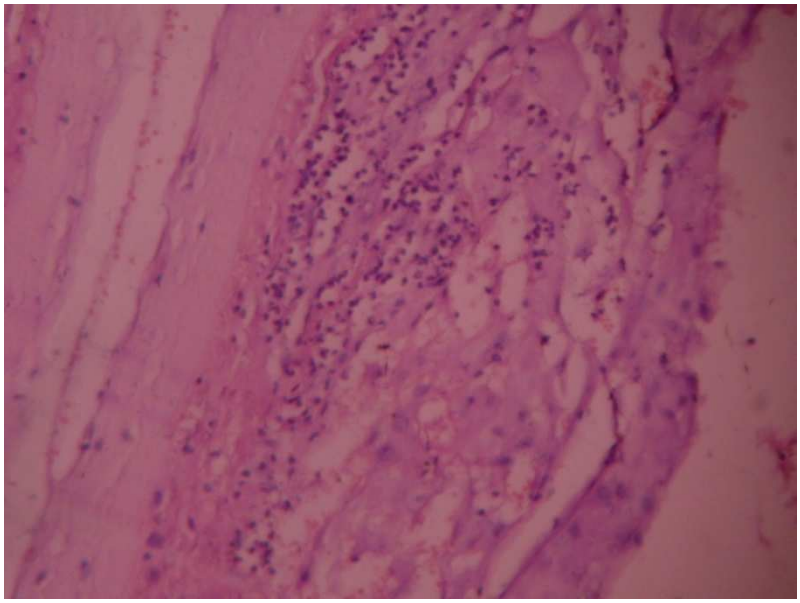
Microscopic picture showing extremely small terminal villi, stem villi are slender with reduced branching

Figure No – 24
Sub Chorionic Micro Abscess



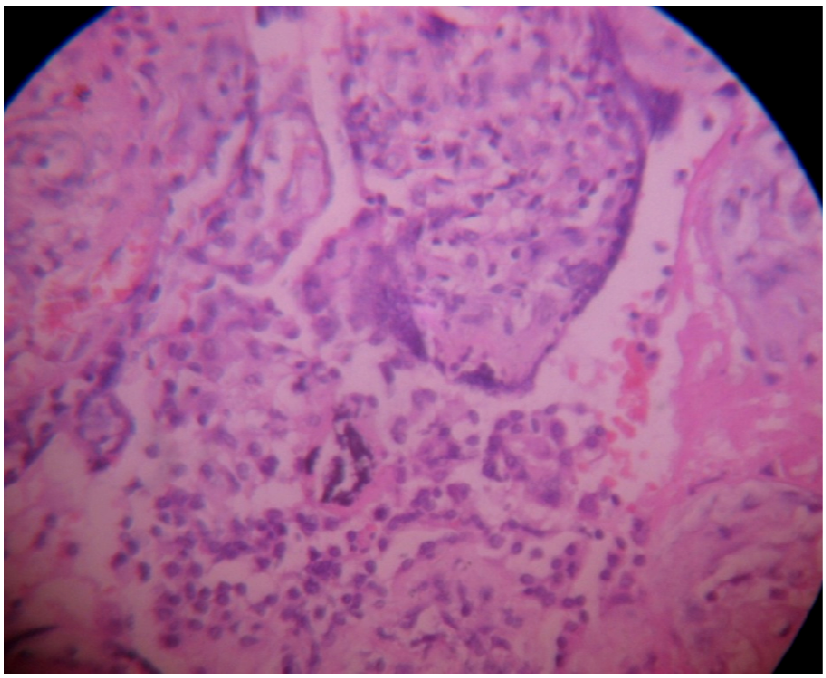
Microscopic picture showing Sub Chorionic Micro Abscess

Figure No – 25
Acute Chorioamniotis- Maternal Inflammatory response stage 1



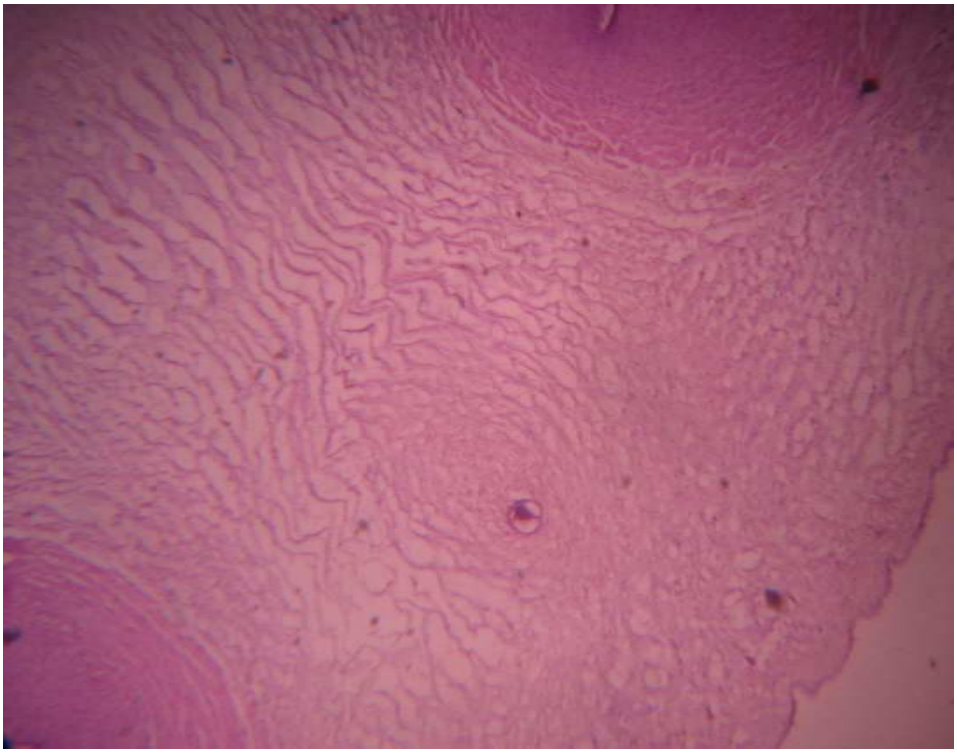
Microscopic picture showing the Chorioamniotis stage 1 - Maternal Neutrophils in the sub chorionic fibrin and at the junction between decidua and chorioamnion

Figure No – 26
Chorionic Intervillositis



Microscopic picture showing chronic inflammatory infiltrates in the intervillous space.

Figure No – 27
Vestigial Remnant



Microscopic picture of umbilical cord showing vitelline duct remnant

ANNEXURE - II
MASTER CHART

S. No	HPR No.	IP Number	Age	High Risk Factors	Gestational Age (in wks)	Birth Weight (in Kgs)	Placental Weight (in gms)	Gross Finding						Histopathology									
								Umbilical Cord			Membrane	Fetal Surface	Maternal Surface	Syncytial Knots	Fibrinoid Necrosis	Intravillous hemorrhage	Villous vasculature	Cytotro-phoblast	Basement Membrane	Vasculo Syncytial Membrane	Stromal Fibrosis	Infarction	Periviloous Fibrin Deposits	Calcification
								Length	Insertion	Vessels														
1	1	52189	24	Anemia	38	1.7	380	44	Peripheral	3	Marginal	Normal	Gray White	>50%	>10%	+	Chorangioma	<20%	>3%	6-30%	<6%	5-9%	0-4%	-
2	2	54976	26	GDM	37	1.6	320	40	Peripheral	2	Marginal	Normal	Gray White	>50%	>10%	+	Normal	20-40%	>3%	<6%	>6%	5-9%	0-4%	-
3	3	57066	28	Oligohydramnios	37	2.3	460	48	Central	3	Marginal Opaque	Normal	Gray White	<30%	>3%	+	Normal	<20%	<3%	6-30%	<6%	-	5-9%	-
4	4	60298	32	-	32	1.5	310	40	Central	3	Marginal	Normal	-	30-50%	>3%	-	Normal	20-40%	<3%	6-30%	<6%	-	0-4%	-
5	5	62448	24	PIH	32	1.45	290	35	Peripheral	3	Marginal Opaque	Normal	Gray White	30-50%	>3%	-	Decreased	<20%	<3%	<6%	>6%	5-9%	5-9%	+
6	6	65705	20	PIH	32	1.12	280	34	Central	3	Marginal Opaque	Normal	Gray White	30-50%	>10%	+	Decreased	<20%	>3%	<6%	>6%	10-25%	5-9%	-
7	7	66201	25	PIH	37	1.5	300	36	Peripheral	3	Marginal	Normal	Gray White	>90%	>10%	-	Normal	20-40%	>3%	6-30%	>6%	5-9%	5-9%	-
8	8	68087	30	-	36	1.15	230	35	Central	3	Circumvallate	Normal	Gray White	<30%	>3%	-	Increased	20-40%	<3%	6-30%	<6%	-	10-25%	-
9	9	69007	26	Oligohydramnios	38	1.2	300	38	Peripheral	3	Marginal	Normal	Gray White	30-50%	>3%	+	Increased	20-40%	<3%	6-30%	>6%	-	10-25%	-
10	10	11038	32	Cervical Incompetence	29	1.25	250	35	Central	3	Marginal	Normal	-	<30%	>3%	-	Increased	20-40%	<3%	6-30%	<6%	-	0-4%	-
11	11	1294	29	-	37	1.36	340	40	Peripheral	3	Marginal	Normal	Gray White	<30%	>3%	+	Decreased	20-40%	<3%	6-30%	>6%	-	>25%	+
12	12	1970	34	-	38	1.44	360	42	Peripheral	3	Marginal Opaque	Normal	Gray White	>90%	>3%	+	Decreased	>40%	>3%	<6%	<6%	-	10-25%	+
13	13	3179	33	Anemia	37	2.25	450	48	Central	3	Marginal Opaque	Normal	Gray White	>50%	>3%	+	Normal	20-40%	>3%	6-30%	<6%	-	5-9%	-
14	14	4550	24	PIH	33	1.5	280	34	Peripheral	3	Marginal Opaque	Normal	Gray White	>50%	>3%	-	Normal	20-40%	>3%	<6%	>6%	5-9%	0-4%	-
15	15	7489	26	-	38	1.2	320	38	Central	3	Marginal Opaque	Normal	Gray White	>70%	>3%	+	Decreased	20-40%	>3%	6-30%	<6%	-	>25%	-
16	16	9708	24	-	37	1.3	330	36	Central	3	Marginal	Normal	Gray White	>90%	>3%	+	Increased	<20%	<3%	6-30%	<6%	-	10-25%	-
17	17	10301	30	Severe Anemia	38	1.5	280	34	Peripheral	3	Marginal	Normal	-	>50%	>10%	+	Increased	20-40%	>3%	6-30%	<6%	-	0-4%	-
18	18	10711	28	-	36	1.6	320	38	Peripheral	3	Marginal	Normal	-	30-50%	>10%	-	Normal	<20%	<3%	6-30%	<6%	-	0-4%	-
19	19	11222	28	Anemia	33	1.5	300	36	Peripheral	3	Marginal	Normal	-	>50%	>3%	-	Increased	20-40%	<3%	>30%	<6%	-	0-4%	-
20	20	11437	30	Anemia	32	1.4	290	35	Peripheral	3	Marginal	Normal	-	>50%	>3%	+	Increased	>40%	>3%	>30%	>6%	-	0-4%	-
21	21	11928	24	PIH	32	1.1	300	36	Peripheral	3	Marginal	SCH	Gray White	>50%	>10%	-	Normal	20-40%	<3%	<6%	<6%	>25%	0-4%	-
22	22	12212	24	PIH	33	1.5	300	38	Central	3	Marginal	Normal	Gray White	>50%	>3%	-	Decreased	20-40%	>3%	<6%	<6%	10-25%	0-4%	-
23	23	12429	28	-	37	1.5	350	38	Peripheral	3	Marginal Opaque	Normal	Gray White	>50%	>3%	-	Decreased	20-40%	<3%	<6%	<6%	-	>25%	-
24	24	13211	26	-	38	1.6	360	40	Central	3	Marginal Opaque	Normal	Gray White	>50%	>3%	-	Decreased	>40%	<3%	6-30%	<6%	-	>25%	-
25	25	22336	26	-	37	1.4	350	41	Central	3	Marginal	Normal	Gray White	>50%	>3%	-	Decreased	20-40%	<3%	6-30%	<6%	-	10-25%	+
26	26	24007	24	Oligohydramnios	37	1.5	380	44	Peripheral	3	Marginal	Normal	Gray White	>50%	>3%	-	Normal	20-40%	<3%	6-30%	<6%	-	10-25%	+
27	27	38412	32	Anemia	33	1.4	250	36	Peripheral	3	Marginal	Normal	Gray White	>50%	>3%	+	Decreased	20-40%	<3%	6-30%	<6%	-	0-4%	-
28	28	40306	24	PIH	31	1.1	260	38	Peripheral	3	Marginal	Normal	Gray White	>50%	>10%	-	Normal	<20%	>3%	6-30%	>6%	5-9%	5-9%	-
29	29	44318	22	PIH	35	1.5	300	39	Central	3	Marginal	Normal	Gray White	>50%	>10%	-	Decreased	20-40%	>3%	<6%	>6%	10-25%	0-4%	+
30	30	48227	25	-	35	1.4	280	35	Peripheral	3	Marginal Opaque	Normal	-	>50%	>10%	+	Decreased	<20%	>3%	6-30%	>6%	-	>25%	+
31	31	55314	22	PIH	33	1.6	340	39	Peripheral	3	Marginal Opaque	Normal	-	>50%	>3%	-	Decreased	20-40%	>3%	<6%	>6%	-	0-4%	-
32	32	59218	31	Anemia	35	1.7	380	40	Peripheral	3	Marginal Opaque	Normal	Gray White	>50%	>3%	-	Normal	20%	>3%	6-30%	<6%	-	5-9%	-
33	33	60218	30	Anemia	37	1.9	420	45	Peripheral	3	Marginal Opaque	Normal	-	>50%	<3%	+	Increased	20-40%	<3%	6-30%	<6%	-	0-4%	-
34	34	62283	24	Diabetes	38	2	400	44	Central	3	Marginal Opaque	Normal	Gray White	>50%	>3%	+	Normal	20%	>3%	6-30%	>6%	-	5-9%	-
35	35	69219	25	Rh -ve/Heart Disease	38	2.4	480	48	Central	3	Marginal	Normal	-	>50%	<3%	+	Increased	20%	>3%	6-30%	<6%	-	0-4%	-
36	36	398	24	GDM	37	2.05	410	46	Central	3	Marginal Opaque	Normal	Gray White	>90%	>10%	+	Normal	20%	>3%	<6%	>6%	-	5-9%	+
37	37	1079	23	Oligohydramnios	36	1.2	370	42	Central	3	Marginal Opaque	Normal	-	>90%	>3%	+	Normal	20%	>3%	<6%	<6%	-	0-4%	-
38	38	1918	28	Anemia	36	1.7	350	44	Peripheral	3	Marginal	Normal	Gray White	>50%	>3%	+	Decreased	20%	<3%	6-30%	<6%	-	5-9%	-
39	39	2906	32	Anemia	37	2.1	480	48	Central	3	Marginal	Normal	-	>50%	>3%	-	Increased	20%	>3%	>30%	<6%	-	0-4%	-
40	40	5216	27	Rh -ve	38	2.25	450	40	Central	3	Marginal	Normal	-	>50%	>3%	+	Increased	20%	<3%	>30%	<6%	-	0-4%	-
41	41	7314	26	Oligohydramnios	37	1.3	350	38	Central	3	Marginal	Normal	Gray White	>50%	<3%	-	Decreased	20-40%	<3%	6-30%	>6%	-	>25%	-
42	42	9245	38	Anemia	32	2	400	38	Peripheral	3	Marginal	Normal	-	>50%	>3%	+	Normal	20-40%	>3%	<6%	<6%	-	0-4%	-
43	43	1129	22	Abruption	33	1.15	350	36	Peripheral	3	Marginal Opaque	Normal	-	>50%	>3%	+	Increased	20-40%	<3%	6-30%	<6%	-	0-4%	-
44	44	19319	30	Twin gestation	32	1.1	220	36	Peripheral	2	Marginal Opaque	Normal	-	30-50%	>10%	+	Increased	20-40%	<3%	6-30%	<6%	-	0-4%	-
45	45	24320	26	Oligohydramnios	35	1.2	300	38	Central	3	Marginal	Normal	Gray White	30-50%	<3%	-	Decreased	20-40%	>3%	<6%	<6%	10-25%	0-4%	-
46	46	28480	30	Twin gestation	32	0.9	230	36	Peripheral	2	Marginal Opaque	Normal	Gray White	30-50%	>3%	-	Normal	20-40%	<3%	<6%	<6%	10-25%	0-4%	+
47	47	32318	22	PIH	34	1.06	280	35	Central	3	Marginal Opaque	Normal	Gray White	>90%	>10%	-	Decreased	20-40%	>3%	<6%	<6%	10-25%	0-4%	+
48	48	38420	36	Anemia	37	1.45	290	39	Peripheral	3	Marginal	Normal	-	>90%	>10%	+	Increased	20-40%	>3%	6-30%	<6%	-	0-4%	-
49	49	44723	25	-	37	2.4	400	45	Central	3	Marginal Opaque	Normal	-	<30%	<3%	-	Normal	20%	<3%	6-30%	<6%	-	0-4%	-
50	50	56218	24	PIH	32	1.2	240	36	Peripheral	3	Marginal Opaque	Normal	Gray White	<30%	<3%	-	Decreased	20-40%	<3%	<6%	>6%	10-25%	5-9%	-

ANNEXURE - I

PROFORMA

PLACENTAL PATHOLOGY IN LOW BIRTH WEIGHT LIVE BIRTHS

Name :

Age :

Address :

Socio Economic Status :

LMP :

EDD :

Parity :

Interpregnancy Interval :

Consanguinity :

History :

H/o Diabetes, Hypertention, Jaundice, Fever, Burning micturition, Antepartum hemorrhage, trauma, irradiation, drug intake, H/o of documented cardiac disease, renal disease etc.,

Investigation :

BP : Urine : Albumin / Sugar

Serology : Hb, HIV, VDRL

Mode of delivery :

Maturity :

Birth Asphyxia : Apgar :

Any congenital anomalies in baby :

ANNEXURE - III

I. Abnormalities of placentation and of placental development

1. Abnormalities of placental shape.

- Placenta extrachorialis
- Placenta membranacea
- Ring-shaped placenta
- Fenestrate Placenta
- Accessory lobe
- Bilobate placenta

2. Placenta Accereta

3. Placenta Previa

4. Placental mesenchymal dysplasia

II. Macroscopic abnormalities of the placenta

A) Lesions due to disturbances of maternal blood flow.

- Perivillous fibrin deposition
- Subchorionic fibrin plaque
- Maternal floor infarction.
- Infarct

B) Lesions due to disturbances of fetal blood flow

- Fetal artery thrombosis (fetal thrombotic vasculopathy)

C) Thrombi & haematomas:

- Massive subchorial thrombosis
- Retroplacental haematoma
- Marginal haematoma
- Intervillous thrombi

- Kline’s haemorrhage
- Subamniotic haematoma

D) Nonvascular lesions:

- Calcification
- Septal cyst

II. Histologic abnormalities of the placenta:

A) Histopathology of the placental villi.

1) Abnormalities of the trophoblast

- Excessive number of syncytial knots.
- Excessive number of villous cytotrophoblastic cells.
- Deficiency of vascular syncytial membranes
- Fibrinoid necrosis of villi.

2) Abnormalities of the trophoblastic basement membrane:

- Increase in its thickness
- Excessive basement membrane mineralization

3) Abnormalities of the stroma

- Stromal fibrosis
- Villous oedema
- Excessive number of villous Hofbauer cells

4) Abnormalities of the villous vessel

- Villous vascularity
- Hypovascularity
- Hypervascularity (Chorangiosis)

5) Generalized abnormalities of the villi.

- Villous immaturity

- Accelerated villous maturation

6) Histopathology of the fetal stem arteries

- Fibromuscular sclerosis
- Obliterative endarteritis
- Hemorrhagic endarteritis / endovasculosis

7) Histopathology of the maternal uteroplacental vessel

- Inadequate transformation of spiral arteries.
- Acute atherosis

BIBILIOGRAPHY

1. Katzman. P.J. and Geenst D.R. (2002) Maternal floor infarction and massive perivillous fibrin deposition: histological definitions, association with intrauterine fetal growth restriction, and risk of recurrence. Pediatric and development Pathology, 5. 159 – 164.
2. Brown, D.L., Di Salvo, D.N., Frates, M.C., Davidson, K.M., and Genest D.R. (2002) Placental surface cysts detected on sonography; histologic and clinical correlation. Journal of Ultrasound in Medicine, 21, 641 – 646.
3. Benirschke, K. and Driscoll, S.G. (1967). The Pathology of the Human Placenta. Berlin, Heidelberg. New York: Springer – Verlag.
4. Mandasagar, N.T., Bendon, R., Mostello, D. et al. (1994) Maternal floor infarction of placenta: prenatal diagnosis and clinical significance. Obstetrics and Gynecology. 83. 750-754.
5. Whittington. S.S. (1998) Clinical correlations of patterns of placental pathology in preterm pre-eclampsia. Placenta, 19. 67 – 72.
6. Fox, H.(1967b)The significance of placental infarction in perinatal morbidity and mortality.Biologica Neonatorum,11,87-105.
7. McDermott,M. and Gillan ,J.E.(1995a)Chronic reduction in fetal blood flow is associated with placental infarction,16,165-170.
8. Redline, R.W. Ariel, I., Baergen, R.N., Desa. D.J., Kraus, F.T.., Roberts, D.J. and Sander, C.M. (2004) Fetal Vascular obstructive lesions; nosology and reproducibility of placental reaction patterns. Pediatric and Development Pathology. 7. 443 – 452

9. Hebich, G.,Bernasconi, M.T.,Gmuer, J., Huch, A. and Stallmach,T. (2000) Pregnancy-associated recurrent haemolytic uremic syndrome with fetal thrombotic vasculopathy in the placenta. American journal obstetrics and gynecology, 185, 1265-1266.

10. Usta, I.M., Abdullah, M. and Nasser, A.H (2004) Massive subchorinic hematomas following by thrombolytic therapy in pregnancy. Obstetrics and Gynecology, 103, 1079-1082.

11. Heller, D.S., Rush, D.S. and baergen, R.N. (2003) Subchorionic hematoma associated with in thrombophilia: report of three cases. Pediatri and developmental pathology, 6, 261-264.

12. Ananth, C.V., Oyelese,Y., Srinivas, N., Yeo, L. And Vintzileos, A.M.(2004)Preterm premature rupture of membranes,intrauterine infection, and oligohydramnios: risk factors for placental abruption. Obstetrics Gynecology,104,71-77.

13. Sheiner, E., Shoham-vardi, I., Hallak, M.et al. (2003) Placental abruption in term pregnancies: clinical significance and obstetrics risk factors. Journal of Maternal, Fetal and Neonatal medicine, 13, 45-49.

14. Parle - McDermott, A., Mills, J.L., Kirke, P.N.et al. (2005) MTHFD1R653Q polymorphism is a maternal genetic risk factor for severe abruption placentae. American Journal of Medical genetics A, 132, 365-368.

15. ANANTH, C.V., Smulian, J.C. and Vintziloes, A.M. (1999a) Incidence of placental abruption in relation to cigarette smoking and hypertensive disorders during pregnancy: a meta-analysis of observational studies. Obstetrics and Gynecology, 93, 622-628.

16. Jaaskelainen, E., Toivonen, S., Rompppanen, E.L.et al. (2004) M385T polymorphism in the factor V gene, but not leiden mutation, is associated with placental abruption in Finnish women. Placenta, 25, 730-734.

17. Darby, M.J.,Caritis, S.N. and shen-schwartz, S. (1989) Placental abruption in the pre term gestation:an association with chorioamnionitis. Obstetrics and Gynecology, 74, 88-92.

18. Gibbs, J.M. and Weidling, A.M.(1994) neonatal intracranial lesions following placental abruption. European journal of Pediatrics,153,195-197.

19. Nagy, S., Bush, M., Stone, J., Lapinski, R.H. and Gardo, S. (2003) Clinical significance of sub chorionic and retroplacental hematomas detected in the first trimester of pregnancy. Obstetrics and Gynecology, 102,94-100.

20. Harris. B.A. (1988) Peripheral placental separation: a review. Obstetrical and Gynecological Survey. 43. 577-581.

21. Desa, D.J.(1971)Rupture of foetal vessels on placental surface. Archives of Disease in Childhood, 46, 495-501.

22. Van den, B.T.,Van Schoubroeck, D., Cornelis, A. And Dubin, M. (2000) Prenatal diagnosis of a subamniotic hematoma. Fetal diagnosis and Therapy, 15, 32-35.

23. Kleges, L.M., Murray, D.M., Brown, J.E., Cliver, S.P. and Goldenberg, R.L.(1998) Relations of cigarette smoking and diatery antioxidants with placental calcification. American Journal of Epidemilogy, 147, 127-135.

24. Graham, E.M., Freedman, L.J. and Forouzan, I. (1998) Intrauterine growth retardation in a woman with primary hyperparathyroidism: a case report. Journal of Reproductive Medicine, 43, 451-454.

25. Hansen, A.R., Collins, M.H., Genest, D. Et al. (2000) Very low birth weight placeta: clustering of morphologic characterisitics. Pediatric and Developmental Pathology. ,, 431-438.

26. Khalid, M.E., Ali, M.E. and Ali, K.Z.(1997) full-term birth weight and placental morphology at high and low altitude. International journal of Gynaecology and Obstetrics., 57, 259-265.

27. Benirschke, K. And Kaufman, P. (2000) Pathology of the human placenta, 4th edn. New York: Springer-Verlag.

28. Buckshee, K., Malkani, P.K. and Khatri, S.(1974)The villous cytotrophoblast as an index of placental dysfunction. In Proceedings of the 6th Asisn Congress of Obstetrics and Gyneacology. Kuali Lumpur, Malaysia. pp. 223-235.

29. Demir, R., Demir,A.Y. and Yinanc, M (1994) Structural changes in placental barrier of smoking mother: a quantitative and ultrastructural study. Pathology Research and Practice, 190, 656-667.

30. Salafia, C.M., Minior, V.K., Lopez-Zeno, J.A. et al. (1995a) Relationship between placental histological features and umbilical cord blood gases in preterm gestation. American Journal of Obstetrics and Gynecology, 173, 1058-1064.

31. Fox, H. (1967a) The incidence and significance of vasculosyncytial membranes in the human placenta. Journal of Obstetrics and Gynaecology of the British Commonwealth, 74,28-33.

32. Wilkin, P. (1965) Pathologie du Placenta. Paris: Masson et Cie.

33. Fox. H. (1968a) Fibrinoid necrosis of placental villi. Journal of Obstetrics and Gynaecology of the British Commonwealth. 75, 448-452.

34. Gershon, R. And Strauss, L. (1961) Structural changes in human placentas associated with fetal inanition or growth arrest (placental insufficiency syndrome). American Journal of Diseases of Children, 102, 645-646.

35. Mayhew. T.M., Brotherton., Holliday, E., Orme, G. And Bush, P.G. (2003) Fibrin type fibrinoid in placentae from pregnancies associated with maternal smoking: association with villous trophoblast and impact on intervillous porosity. Placenta, 24, 501-509.

36. McDermott, M. And Gillan, J.E. (1995) Trophoblast basement membrane hemosiderosis in the placental lesion of fetal artery thrombosis: a marker for disturbance of maternofetal transfer Placenta, 16,171-178.

37. Roberts, l., Sebire, N.J., Fowler, D. and Nicholaide, K.H. (2000) Histomorphological features of chorionic villi at 10-14 weeks of gestation in trisomic and chromosomally normal pregnancies. Placenta, 21, 678-683.

38. Ernst, L.M. and Parkash,V. (2002) Placental pathology in fetal Bartter syndrome. Pediatric and Developmental Pathology, 5, 76-79.

39. Ghidini. A., Pezzullo.J.C., Sylvestre.G., Lembet.A. Salafia, C.M. (2001) Antenatal corticosteroids and placental histology in preterm birth. Placenta, 22, 412 – 417.

40. Fox, H. (1968c) basement membrane changes in the villi of the human placenta. Journal of Obstetrics and Gynaecology of the british Commonwealth, 75, 302 – 306.

41. Younes, B Baez – Giangreco, A., al Nuaim, L., al Hakeem, A. and Abu, T.Z. (1996) Basement membrane thickening in the placentae from diabetic women. Pathology International, 46, 100 – 104.

42. Fox, H. (1968b) Fibrosis of the placental villi. Journal of pathology anf bacteriology, 95, 573 -579.

43. Ilagan, N.B., Elias, E.G., Liang, K.C. et al. (1990) Perinatal and neonatal significance of bacteria-related placental villous edema, Acta Obstetricia et Gynecological Scandinavica, 69, 287 – 290.

44. Tarjan, G. (1965) placentardem in der Toxaemia. Archiv fur Gynkologie, 202, 262 – 263.

45. Gruenwald, P. (1961) Abnormalities of placental vascularity in relation York State Journal of Medicine, 61, 1508 – 1517.

46. Emmrich. P. and Mulzer, G. (1968) zur Morphologie der Plazenta bei auubertragung. Pathologia et Microbiologia. 32, 285 – 302.

47. Altshuler, G. (1984) Chorangiosis: an important placental sign of neonatal morbidity and mortality. Archives of Pathology and Laboratory Medicine.108,71-74.

48. Ogino, S. and Redline, R.W. (2000) Villous capillary lesions of the placenta: distinctions between chorangioma, chorangiomatosis, and chorangiosis. Human Pathology, 31, 945 – 954.

49. Altshuler, G. (1991) The Placenta. In Surgical Pathology of the Female Reproductive System and Peritoneum. Sternberg, S.S. and Mills, S.E., (Eds), pp. 17 – 36. New York: Raven Press.

50. Benirschke, K. (1994) Placenta pathology questions to the perinatologist, Journal of Perinatology 14, 371 – 375.

51. Balci, S., Aypar, E., Altinok, G., Boduroglu, K. And Beksac, M.S. (2001) Prenatal diagnosis in three cases of iniencephaly with unusual postmorterm findings, Prenatal Diagnosis, 21, 558 – 562.

52. Smith, A.S, Hugang, W.Y., Wong G. And Levine, D. (2003) Placental chorangiosis associated with markedly elevated maternal chorionic gonadotropin: a case report. Journal of Reproductive Medicine, 48, 827 – 830.

53. Fujikura, T. And Benson, R.C, (1964) Placentitis and fibrous occlusion of fetal vessels in the placentas of stills-born infants. American Journal of Obstetrics and Gynaecology 89, 225 - 229.

54. Becker, V. and Dolling, D. (1964) Gefassverschlusse in der PLazenta bei Totgeborenen. Virchows Archiv fur pathologische Anatomie und Physiologie und fur klinische Medizin, 338, 305 – 314.

55. Dring, W. And Kloos, K. (1964) Morphologische Routine – diagnostic der Placenta. Munchener Medizinische Wochenschrift. 106, 1849 – 1855.

56. Fox, H. (1968d) Villous immaturity in the term placenta. Obstetrics and Gynaecology, 31, 9-12.

57. Becker, V. (1975) Abnormal maturation of villi. In The Placenta and Its Maternal Supply Line. Gruenwald, P. (Ed.), pp. 232 – 243. Lancaster: Medical and Technical Publishing.

58. Kraus, F.T., Redline, R.W., Gersell, D.J., Nelson, M.D. and Dicke, J.M. (2004) Atlas of Nontumor Pathology. Placental Pathology. Washington D.C., American Registry of Pathology and Armed Forces Institute of Pathology.

59. Evers, I.M., Nikkels, P.G., Sikkema., J.M and Visser, G.H. (2003) Placental pathology in women with tyoe 1 diabetes and in a control group with normal and large – for – gestational – age infants, Placenta, 24, 819 – 825.

60. Schuhmann, R. and Geier, G. (1972) Histomorphogische PLacentabefunde bei eph – gestose. Ein BEitrag zur Morphologie der insuffizienten Placenta. Archiv fur Gynakologie, 213, 31 – 47.

61. Schuhmann, R. (1975) Reifungsstrungen der Plazenta. Archiv fur Gynakologie, 219, 357 – 360.

62. R.D. Virupaxi et al, Morphology of placenta and its relation with small for date babies in 950 live births, recent search in science, technology 2011, 3(2): 123 – 126.

63. Aparna Narasimha, D.S. Vasudeva. Indian Journal of Pathology and Microbiology – 54 (1) January – March 2011.

64. Mallik GB, Mirchandani JJ, Chita S. Placenta in intrauterine growth retardation. J Obstet Gynaecol India 1079:29:805-10

65. Nobis P, Das U, Placental morphology in hypertensive pregnancy. J Obstet Gynaecol 1990:40:166-9.

66. Bhatia A, Shama SD, Jalnawalla SF, Sagreiya K. A comparative study of placental and fetal outcome, India Pathol Microbiol 1981:24:277 -83.

67. Cullen TS. Embryology, Anatomy and Disease of the Umbilicus, 1916, W.B. Saundes. Philadelphia, PA.

68. Hathout H. The vascular pattern and mode of insertion of the umbilical cord in abortion maternal 1964, 71 : 963 – 64.

69. Sepulveda W, Bower. S, Falck NJ, Fik NM Dicord and Iliac and femoral artery flow velocity waveforms in fetuses with SUA Am J Obstet Gynecol 1995; 173: 728 – 32.

70. Driscoll SG, Antenatal infection and unruptured membranes. Pediatrics 1970; 45:886 – 9.

71. Thomas, D., Makhoul, J, and Muller, C. (1992) Fetal growth redartation due to massive subchorionic thrombohematoma: report of two cases. Journal of Ultrasound in Medicine, 11, 245 – 797.

72. Kher AV, Zawar MP. Study of placental pathology in toxemia of pregnancy and its fetal implications, India J Pathol Microbiol 1981:24:245 – 51.

73. Labarere C, Althabe O, chronic villitis of unknown aetiology in recurrent intrauterine fetal growth retardation placenta 1987; 8: 167 – 73.

74. Becoft PM, Thomson JMD, Mitchell EA. The epidemiology of placental infarction at tem. Placenta 2002; 23: 343 - 51.

75. Pardi 9, Marconi AM, Cetm I, Placental fetal interrelationship in IUGR features. Placeta 2002; 23: 136-41.

76. Karsdorp VHM, Pirks BK, Van der Linden JC, Van Vugt JM4, B eak JPA, Van Geijn HP. Placenta Morphology and absend on reversed and diastolic flow velocities in the umbilical artery: a clinical and morphometrical study, placenta 1996; 17: 393 – 9.

77. Mirchandani JJ, Mallik GB, Chitra S. Correlation of foetal outcome with some pathological changes of placenta.J Obstet Gynaecol India 1979:29:1131-9.

78. Shankim DR. The influence of placental lessons on the newborn infant. Pediatrics clin North Am 1970; 17 (1): 25 – 42.

79. Fox H. General pathology of the placenta. In: Fox H, editor. Haines and Taylo Obstetical and Gynecological Pathology. 4th ed. Edinbugh: Chuchill Livingstone: 1995. P. 1480 – 2.

80. Masodkar AR, Kalamkar LR. Patke PS. Histopathology of placenta and its correlation with fetal outcome. J Obstet Gynaecol India 1985:35:294 – 7.

81. Sodhi S. Mohan H, Jaiswal TS, Mohan PS, Rathee S. Placental pathology in pre – eclampsia eclampsia syndroms. Indian J Pathol Microbioi 1990 : 33: 11– 6.

82. Fox H. Basement membrane changes in the villi of the human placenta. J Obstet Gynaecol Br Commonw 1968:102:347 – 53.

83. Mucitelli DR, Charles EZ, Kraus FT. Chorio- an – giomas of intermidate size and intrauterine growth retardation. Pathol Res Pract 1990;186:455 – 8.

84. Kingdom JC, Rodeck CH, Kaufmann P. Umbillcal artery Doppler – more harm than good? Br J Obstet Gynaecol 1997 ; 404: 393 – 6.